EXHIBIT 21

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF NEW YORK

JEANETTE ALLEYNE, *et al.*,

Plaintiffs,

-against-

NEW YORK STATE EDUCATION DEPARTMENT, *et al.*,

Defendants.

AFFIDAVIT OF EDWARD A. SASSAMAN, M.D.

Civ. A. No. 1:06-CV-994-GLS

AFFIDAVIT OF EDWARD A. SASSAMAN, M.D.

I, Edward A. Sassaman, M.D., upon my own personal knowledge, hereby depose and declare the following:

1. I am a Physician licensed to practice in the Commonwealth of Massachusetts and the State of New York and I am board certified in the field of Pediatrics. I currently serve as the Regional Medical Director for Excellus BlueCross BlueShield in Rochester, New York and have been appointed an Expert Reviewer in Pediatrics by the Office of Professional Medical Conduct in Albany, New York.

2. I have been retained as an expert witness by the Plaintiffs in the above-captioned action.

3. I have authored a written report entitled "Expert Medical Report Re: *Alleyne, et al. v. New York State Education Department, et al.*" ("Report"), based upon my review of detailed written records and other information and my activities as set forth in the Report. A true

and accurate copy of the Report, which was provided to Defendants' counsel on April 14, 2008, is attached hereto as Exhibit 1, and is incorporated herein by reference.

4. All of the statements and opinions in the Report are true. I offer all of these opinions and conclusions to a reasonable degree of medical certainty.

SWORN TO AND SIGNED UNDER THE PAINS AND PENALTIES OF PERJURY ON THIS ___ DAY OF MARCH, 2009.

/s/ Edward A. Sassaman, M.D.
Edward A. Sassaman, M.D.

Sworn to before me this

March 26, 2009

/s/
Notary Public

EXHIBIT 1

The material attached as Exhibit 1 is confidential and the Court has given leave for it to be filed traditionally and under seal.

DR. EDWARD A. SASSAMAN, M.D.

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Rochester, NY 14647
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Re: *Alleyne, et al. v. New York State Education Department, et al.*

I have been retained by Michael P. Flammia, Esq. of Eckert Seamans Cherin & Mellott, LLC, and asked to provide expert medical testimony in the above stated case. In preparation for drafting this response, I reviewed the New York State regulations on aversive interventions, the medical files for each of the JRC students identified as representative plaintiffs, and visited JRC for the purpose of conducting annual physical examinations in February of 2008. (Please see relevant medical reports attached as Exhibits 1 thru 9.) I have extensive knowledge of JRC's success in treating some of the most behaviorally-involved individuals in the country and therefore consider myself to be more than adequately qualified to testify regarding the potential medical impact that these proceedings may have upon New York students.

I am a physician licensed to practice medicine in the states of New York and Massachusetts and I am board certified in the field of Pediatrics. After completing my undergraduate studies, I graduated from Harvard Medical School and completed both my residency and fellowship at Children's Hospital Medical Center in Boston, Massachusetts. I currently serve as the Regional Medical Director for Excellus BlueCross BlueShield in Rochester, NY and have been appointed an Expert Reviewer in Pediatrics by the Office of Professional Medical Conduct in Albany, NY. My curriculum vitae is attached as Exhibit 10.

I first became involved with the student population at the Judge Rotenberg Educational Center ('JRC') in 1981 when I began serving as the school's Medical Director. For approximately 5-6 years, I was responsible for the daily oversight of the students' medical needs and spent time at both the residences and the school's main facility which was then located in Providence, RI, and doing business under the name of Behavior Research Institute ('BRI'). During this same time, I was also serving as the Associate Director of the Child Development Center which functioned as a federally and state-funded multi-disciplinary clinic for handicapped children. In 1984, I moved to Springfield, Massachusetts, where I practiced as a pediatrician and subsequently accepted a position as the Director of Pediatrics at Kaiser Permanente. When it became obvious that the travel between western Massachusetts and the school was becoming too burdensome, it became necessary for me to resign as BRI's Medical Director. I have functioned as a Medical Consultant ever since.

In my role as a consultant to JRC, I conduct yearly exams, visit the school one weekend every month or two for the purpose of evaluating students, examine new students upon admission to the program, review records, and receive updates regarding any pertinent medical issues. I maintain constant contact with the Medical Staff and speak with the Coordinator of Medical Services, Doris Baron, RN, on an almost daily basis. Through these phone calls, I am made aware of any significant medical issues and have made myself available via phone and email 24 hours per day. In the event that a JRC student is admitted to the hospital, I have spoken with attending physicians and have closely followed the urgent care needs of the hospitalized individual.

I have over 25 years of familiarity with aversive procedures and am aware of the medical aspects of the treatment modalities in use at JRC. During my time at JRC, I have personally seen hundreds of students who have received aversive treatment procedures such as the Graduated Electronic Decelerator ('GED'), the GED-4, movement limitation, helmet, specialized food and contingent food. I have never seen any physical harm resulting from the use of aversive treatments, other than, in some cases, a very minor reddening and/or appearance of a scab on the skin site associated with the application of the GED device.

In my opinion, which I hold to a reasonable degree of medical certainty, the New York State Education regulations regarding aversive procedures are not necessary to preserve student health and safety and minimize physical and emotion harm. In many ways, these regulations are actually counter-productive. As stated previously, I have never seen physical harm from the use of the aversives, other than, in some cases, a very minor reddening and/or appearance of a scab on the skin site associated with the application of the GED device. Furthermore, I have often spoken with higher functioning students who invariably tell me that once their behavior is under control through aversives; they feel calmer and better able to function in the school and community. (See medical report for T.J. attached as Exhibit 4.) These requirements would in fact cause harm to a child suffering from severe behavior disorders and would preclude them from the obvious benefit of participating in an appropriate educational experience. If these behaviorally-involved children are not allowed access to aversive interventions, they will not be afforded the most appropriate form of treatment available. They will instead be relegated to a future filled with potentially harmful prescription medications. The NYSED regulations do nothing to preserve the public health and safety and do nothing to avoid the risk of physical injury or emotional harm.

The basis for my opinion is as follows. Through my education and training and numerous years of experience treating children who suffer from severe behavior disorders, it is abundantly clear that there exists a small population of children who suffer from severe behavior disorders that cause them to attack others, engage in self-abuse, destroy property, disrupt their environment and completely refuse to participate in family, social and educational activities. These individuals are unable to be effectively served in public schools and are often referred to specialized programs such as JRC. What sets JRC apart from other NY-approved programs, is that JRC is able to effectively treat the most involved students with the most dangerous and life-threatening behaviors. Successful

treatment of this population requires a behavior modification treatment plan with aversive interventions such as those offered at JRC including the GED, GED-4, movement limitation, contingent food and specialized food. JRC uses these aversive interventions safely and effectively to treat aggressive, health-dangerous, disruptive, destructive and non-compliant behaviors in children who could not be effectively treated with drugs and other available interventions in New York and other states.

In my opinion, which I hold to a reasonable degree of medical certainty, a complete ban on the use of aversive interventions would leave a very specific population of individuals without any effective treatment options. If aversives were completely banned after June 30, 2009, the school would have enormous difficulty helping the students. Because there are no effective alternatives, as shown by the fact that these options have all been tried prior to their admission to JRC, the affected students would suffer severe emotional and physical harm and receive no educational benefit. Without access to the effective treatment options that are currently available at JRC, individuals with severe behavior disorders will likely end up heavily medicated, institutionalized and, in some cases, involved with the judicial system. Medically, those students with the most severe self-abusive behaviors may succeed in blinding, permanently maiming or actually killing themselves.

The basis and reasons for this opinion are my medical education and training in pediatrics, my extensive experience with developmentally disabled children and adults, the 27 years I have spent treating students at JRC, and my monthly exams and visits with the students at JRC.

In my opinion, which I hold to a reasonable degree of medical certainty, the restrictions on the use of aversives contained in the NYSED regulations would likely cause harm to a student with a severe behavior disorder who is in need of aversive interventions. These restrictions, if imposed on the JRC students, would unnecessarily diminish the effectiveness and benefits of the aversive interventions. Of particular concern are the following sections of the New York regulations:

8 NYCRR §200.22 (e)(1):

> *"Aversive interventions shall be considered only for students who are displaying self-injurious and/or aggressive behaviors that threaten the physical well being of the student or that of others, and only to address such behaviors."*

By limiting aversive treatment to aggressive and health dangerous behaviors, NYSED Regulations allow minor behaviors to escalate. Many times in the 27 years that I have been treating students at the JRC, I have seen minor behaviors (such as hand to mouth) quickly escalate to major behaviors such as eye poking or head banging. By treating the "minor" antecedents to severe self-injurious behavior ('SIB'), I have witnessed those severe, life-threatening behaviors dramatically diminish.

8 NYCRR §200.22 (e)(2):

"No child-specific exception shall be granted for interventions used as a consequence for behavior which are intended to induce pain or discomfort that include ... use of an automated aversive conditioning device, ..."

By preventing automated aversive conditioning devices, NYSED Regulations are actually promulgating SIB. Several times I have seen head banging or hitting eliminated by keeping the hands in a "holster-like" device. Also, by conditioning a student to remain in his/her classroom seat, I have seen severe acting out behaviors eliminated.

8 NYCRR §200.22 (e)(2):

"...the combined simultaneous use of physical or mechanical restraints and the application of an aversive intervention, ..."

AND

8 NYCRR §200.22 (f)(2)(ix):

"No program may combine the simultaneous use on a student of a physical or mechanical restraint device with another aversive intervention."

By preventing restraint and aversives at the same time, NYSED Regulations actually lengthen the time in restraint, which to me is the most intrusive form of treatment. By appropriately using aversives while a student is in restraint, I have many times seen restraint times significantly shortened.

8 NYCRR §200.22 (f)(2)(vii):

"Whenever possible, the use of aversive interventions shall apply the lowest intensity for the shortest duration and period of time that is effective to treat the problem behavior and employ strategies that increase the effectiveness of mild levels of aversive interventions. In the event the aversive intervention fails to result in a suppression or reduction of the behavior over time, alternative procedures shall be considered that do not include increasing the magnitude of the aversive intervention."

This is actually a semantic question. To apply an aversive at the lowest intensity for the shortest time period might initially stop a behavior, but the intensity and time period would need to be adjusted because of rapid habituation. The intensity and time need to be adequate so that habituation does not occur.

8 NYCRR §200.22 (f)(2)(viii):

"The use of any aversive conditioning device used to administer an electrical shock or other noxious stimuli to a student to modify undesirable behavioral

characteristics shall be limited to devices tested for safety and efficacy and approved for such use by the United States Food and Drug Administration where such approval is required by federal regulation. The magnitude, frequency and duration of any administration of aversive stimulus from such a device must have been shown to be safe and effective in clinical peer-reviewed studies. The use of automated aversive conditioning devices is prohibited."

Decades worth of internal studies at the JRC have shown the aversives, including the GED and GED-4, to be safe and effective. I have examined hundreds of students after aversive treatment, including GED and GED-4, and have never seen any short or long-term consequences of any clinical significance.

The basis for my opinions regarding the NYSED regulations and their potential harmful effects on JRC's students remain as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, other effective alternatives to aversive procedures do not exist because, prior to their admission to JRC, numerous other forms of treatment have been tried without any real success. As previously mentioned, most students are admitted to JRC on numerous psychotropic medications. These students have failed in multiple other programs (inpatient and outpatient) which have included close pharmacologic supervision by psychiatrists. In fact, histories of the plaintiffs in this case reveal that they had all been prescribed numerous medications prior to their admission to JRC, with no real effect. There are no safe alternatives to the JRC program.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, the health and educational progress of a student who needs aversives and cannot receive them due to the NYSED regulations would suffer significantly. Students who cannot receive aversive therapy because of the NYSED regulations will be at significant risk for grave deterioration in their physical and emotional state. The overall physical, emotional, and behavioral conditions of the students admitted to JRC demonstrates the need for these alternative treatments and are, in many cases, the reasons why a child is referred to the program. Prior to the implementation of behavioral treatment plans containing aversive procedures, many of these children had not previously cooperated with routine medical and dental prophylaxsis. Currently, each of the plaintiffs in this case is in good, general health and is behaviorally able to cooperate with medical examinations.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, students with severe behavior problems who cannot receive appropriate aversive therapy for their most disruptive, destructive, or non-compliant behaviors have a grave prognosis. Ultimately, the student will not learn replacement behaviors, and these disruptive, destructive, or non-compliant behaviors behaviors will most likely escalate into aggressive and health-

dangerous behaviors. These resulting behaviors may then cause the student to be removed to a separate classroom away from his/her classmates which in turn will hinder the child's social development.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, the students will suffer irreparable harm if the NYSED Regulations are enforced against them. As stated above, permanent physical damage to the students will likely result if these treatment procedures are no longer available. These students would probably be prescribed medications which would subject them to the side-effects associated with psychotropic medications. The behaviors will continue and the students will not receive the appropriate education to which they are entitled.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, parents and guardians who have passed the JRC parent training program should be allowed to use the GED and GED-4 devices during home visits. In many cases, parents who had been afraid of the unpredictability and seriousness of their child's behaviors were forced to stay in their homes and not experience opportunities in the community. Effective treatment during home visits allows the parent and child to have a better relationship and for many, allows the family to successfully interact with their community for the first time. In those cases where the parents and guardians have successfully completed the training program and continue the child's program during a home visit, there is continuity of treatment across all environments and less of a chance that the child's behaviors will regress. Many times I have seen a marked increase in self-injurious behavior in students returning from home visits where aversives were not used.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, access to aversives is definitely necessary for the health, well-being and education of the child. When combined with positive programming and a structured behavioral program, aversive interventions are absolutely critical for children who present with severe behaviors. With these interventions in place, their self-abusive, aggressive, destructive, major disruptive and non-compliant behaviors will decrease and they will not suffer from the physical or emotional damage that have plagued them for most of their lives. These children have already been failed by the educational system and without the availability of these procedures, many will end up heavily medicated and far removed from a typical classroom setting. These individuals will most likely still be exhibiting serious behaviors, thereby resulting in no social interaction and no appropriate education.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, JRC's diet and nutrition program is excellent. In fact, the diet in place at JRC is one of the healthiest dietary options available. The menu offered at JRC meets all USDA requirements and, although primarily vegetable based in nature, allows for meat supplements 4-5 times per week. Even without taking advantage of these meat options, the diet still meets all federal and state standards. As a result of a generally unhealthy lifestyle, psychotropic medication side effects, or from excessive periods of inactivity resulting from over-medication, many students are admitted to JRC with significant weight issues. Some have already been diagnosed with Type II Diabetes prior to their admission. With the help of the diet/exercise program in place at JRC, these students gradually lose weight, and have been taken off of their medications by their endocrinologists at Children's Hospital, Boston. Their laboratory studies have improved dramatically and a Student Cholesterol Study conducted at the school produced some amazing results. Students are regularly weighed, with Body Mass Index ('BMI') and calories monitored by a nutritionist. JRC's healthy diet and concentration on a healthy lifestyle encourages the students to make healthier choices.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, there are no medical or emotional adverse side-effects from the skin shock devices used at JRC or any other aspect of JRC's program. In my 27 years of experience consulting for JRC and the many physical examinations of the students, I have not seen any adverse side effects other than, in some cases, a very minor reddening and/or appearance of a scab on the skin site associated with the application of the GED device. In these cases, however, the minor skin issues healed quickly and did not result in any lasting effects. When applied as part of a structured and consistent behavioral treatment plan, aversive interventions pose no medical risks to the students. I have extensive knowledge of the aversive procedures used at JRC and feel that the students have received tremendous benefits from this form of treatment.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, there are no medical or emotional adverse side-effects from the Contingent Food Program or the Specialized Food Program used at JRC. All necessary precautions are followed prior to implementing either of the food programs and numerous safeguards are in place to ensure that students are receiving adequate nutrition. Weights and caloric intake are followed closely to help move students to recommended ideal BMI as proposed by the Centers for Disease Control and Prevention ('CDC'). The routine inspections by the Nursing staff help to insure that the target weights for each student are maintained. An appropriately qualified consulting nutritionist will provide follow-up as needed.

The basis for my opinion is as stated above.

In my opinion, which I hold to a reasonable degree of medical certainty, JRC takes all

necessary medical precautions in implementing aversive interventions as part of a student's behavior modification treatment program. A physician will conduct an initial examination of each student for whom the use of aversive procedures is being proposed. After the physical review of the student and a review of his/her records, the physician will make a determination as to whether any of the proposed interventions would be contra-indicated for that particular student. JRC will not pursue court approval of any aversive procedures that have been contra-indicated by the examining physician.

The basis for my opinion is as stated above.

I have not authored any publications within the preceding ten years, nor have I testified as an expert witness at trial or by deposition in the past four years. My hourly rate of compensation is $175, which will serve as my fee for both this study and my testimony.

Prepared by:

Edward A. Sassaman, M.D.
April 10, 2008

Exhibit I

D[redacted] B[redacted]
DOB: [redacted]

D[redacted] is a 14 year old young man with behavioral difficulties and developmental delay. D[redacted] was admitted to the JRC approximately four years ago. Medications prior to arrival included Wellbutrin. D[redacted] began on aversive interventions in January 2006. Prior to that time he had severe self-injurious behavior as part of his health dangerous behaviors. He also refused medications and treatments. The most significant issue was suicide threats. He began aversive interventions in January 2006. Shortly thereafter the health dangerous behaviors almost disappeared, and he has now been faded from the GEDs. He's no longer being restrained, and he's working in his classroom with an IEP. The suicidal ideation is gone.

He currently is in excellent health. Certainly, he's not been harmed physically or emotionally by the aversive intervention. Indeed, he's made significant progress. He's suffered no negative side effects from the aversive interventions. He did have some questionable scabs that have seen as associated with GEDs, but these healed over quite quickly and really have left no side effects.

The quality of his life has improved dramatically because of aversive intervention. His health dangerous behavior is in essence gone, and he's able to participate in classroom activities as well as community based activities.

I'm unaware of any effective alternative treatments that could be used with D[redacted] since they have been used in the past and have been ineffective with the exception of the aversive intervention at school. If he did not have access to these aversive interventions, I'm concerned that he would not be able to participate in the classroom or community and might be living a much more restrictive life.

Edward Sassaman, M.D.

Exhibit 2

J[redacted] B[redacted]
DOB: [redacted]
DOA: [redacted]2005

J[redacted] is an 18 year old young man with autism, mental retardation, and seizures. J[redacted] currently is in good health. When he arrived at the JRC he was in good routine health. He had been on a variety of medications in the past including Loratadine, Trileptal, and Risperdol. He had no abnormalities on blood work from his psychotropic medications, and his exam on admission was normal. J[redacted] had severe health dangerous behaviors on admission including severe self-injurious behavior with head banging, biting and pulling his hair.

He was started on the GED program in February 2006, and his severe health dangerous behaviors disappeared almost at once. He's continued to do quite well since then. He currently is functioning quite well in the classroom in an IEP diploma program and is able to partake in community based activities.

He's able to cooperative with all medical appointments, both in the school and in the community, and in addition, he's able to participate in dental prophylaxsis. He was able to do neither of these prior to the institution of the GED program. He's had no side effects whatsoever from the aversive interventions. Since none of the alternative treatments that were tried prior to his arriving at the JRC were effective, I seriously doubt that they would any more effective now. If he had not been admitted to the JRC and been able to be programmed with the aversive interventions, he certainly would not have been able to cooperate with routine medical and dental prophylaxsis, nor would he be able to be working toward an IEP diploma and participate in community based activities. There's no question that the aversive interventions have had a dramatic impact on the quality of his life.

Edward Sassaman, M.D.

Exhibit 3

J[redacted] H[redacted]
DOB: [redacted]

J[redacted] is a 17 ½ year woman with behavior problems and developmental delay. She currently is in good health. J[redacted] was referred to the JRC because of severe behavior problems. She had been on numerous medications in the past prior to arrival including Seroquel, Strattera, and Risperdol. On admission, she did have abnormal liver function studies very possibly secondary to her previous of psychotropic medications. The abnormal liver function studies have since reverted to normal.

J[redacted]'s major health dangerous behavior was aggression towards others and self-injurious behavior. She also had runaway behavior. She was extremely difficult to exam initially, and her initial physical exam had to be done by me while she was basically in restraint. Use of the aversive interventions began in June and immediately a dramatic difference was noted in her aggression towards others and her self-injurious behavior. She currently can be examined without any difficulties and has been off of the GED for a few months. She is now able to attend classes outside of the school at Blue Hills Community College. There is no question that J[redacted] has made tremendous progress with a dramatic improvement in the quality of her life as evidence by her ability to pursue educational opportunities in the local community college.

Alternative treatments were not effective with J[redacted] in the past and there is no reason to suspect that they would be effective now. If she had not had access to the aversive interventions used at the school. She certainly would not be able to attend college and in all probability would be back on numerous psychotropic medications in various much more restrictive environment. J[redacted] is able to comply with all health appointments now and fully cooperative with all health professionals, both in the school and in the community.

Edward Sassaman, M.D.

Exhibit 4

T[redacted] J[redacted]-A[redacted]
DOB: [redacted]
DOA: [redacted]-2005

T[redacted] is an 18 year old young man with a long history of developmental delay and severe behavior problems. T[redacted] is in good health now. He came to the school having been on numerous medications in the past including Valproic Acid, Clozaril, Klonopin, Neurontin, Haldol, Zyprexa, Seraquil, and Clonidine. He currently is on no medications. He has an allergy to Lithium. When he came to the school, he had a low white blood count and low platelet counts possibly secondary to medication. He was admitted on Cogentin, Clozaril, Valproic Acid, and Clonidine and gradually tapered off of those medications.

His most severe health dangerous behavior was suicide threats and runaway behavior, both verbal and actual, with acting out behavior towards others. He began on the GED program in November 2005 and shortly thereafter those behaviors were gone. I asked T[redacted] how he feels about the GED and if it helped him, and his response was "It helped me a lot. I learned right from wrong; not to attach people; that I can't assault someone; and there's no point in doing the wrong thing. I think positive and do what I need to do and then move on."

T[redacted] is in the classroom working towards his GED and participating in community based activities. He's able to attend all school and community health appointments with no problems. He's had no side effects whatsoever from the aversive therapy, and there's no question that he's had dramatic improvement in the quality of his life as evidence by his own quote. I know of no alternative treatment that would be effective with T[redacted] since he's been on numerous medications in the past prior to arriving at the school and while at the school that had no effect whatsoever. If he were not able to participate in the aversive program at the JRC, I'm afraid that T[redacted] probably would have continued his severe self-injurious behavior and acting out behavior, and very possibly would be under the direct supervision of the judicial system now.

Edward Sassaman, M.D.

Exhibit 5

C[redacted] L[redacted]
DOB: [redacted]
DOA: [redacted]2001

C[redacted] is a 16 year old young man with autism, pervasive developmental delay and mental retardation. C[redacted] was admitted to the school when he was nine years old. His past history is significant for severe self-injurious behavior and numerous placements. Medications in the past had included Valproic Acid, Klonopin, Ritalin, and Risperdol. His medication on admission was Risperdol, which was quickly discontinued.

C[redacted]' major problem was severe health dangerous behavior including self-injurious behavior, eating inedibles, putting his fingers in light socks and picking soars on his fingers. He began the GED in November 2001, and those behaviors disappeared almost immediately. Since then, his behavior has been remarkable good. He remains in excellent health. He has had no side effects whatsoever from aversive therapy. He's now able to participate in classroom and community based activities. If he had not been able to participate in programming here at the JRC, I suspect that he would be on numerous medications with the potential for significant side effects. Certainly it is unlikely that he would be able to participate in school and community programs the way he is able to now.

I can think of no effective treatment other than the programming here at the JRC since C[redacted] had been in numerous programs with numerous types of medications in the past and none of them were effective. C[redacted] is now able to attend all school and community health activities including dental evaluations with absolutely no problems. This certainly was not true previous to beginning the aversive programming here at the JRC.

Edward Sassaman, M.D.

Exhibit 6

G[redacted] R[redacted]
DOB: [redacted]

G[redacted] is a 10 year old young girl with autism and mental retardation who has been a student at the JRC since [redacted] 2005. When G[redacted] was admitted, she had a long history of mental retardation and autism with severe behavior problems. She'd been in a variety of special education and mental health placements.

At time of admission, G[redacted] was on Rispredal, Clonidine, and Geodon. Her physical exam at time of admission was normal as were laboratory values. Physical examination was preformed with great difficulty. Since admission to the JRC, G[redacted] has been tapered off of medications. Since being started on an aversive program on 3-15-2007, G[redacted] has improved considerably. She had a history of significant health dangerous behaviors including eating inedibles, self-injurious behaviors, smearing feces, and poking her eyes, as well as refusing medication. Her non-compliance was quite significant. Now while on aversive therapy, her health dangerous behaviors have decreased dramatically. Today's physical exam was preformed with minimal difficulty. She has suffered no side effects from aversive interventions as determined by routine physical examinations, as well as numerous examinations for routine health issues.

In my opinion, G[redacted] has had a significant improvement in the quality of her life because of the aversive interventions used at the JRC. These have allowed her to cooperate with medical examinations by specialized, as well as routine medical examinations and take medications for period routine child health issues. If she did not have access to these aversive interventions, I'm sure that she would be on significant doses of psychotropic medications which at best did not work previously and at worst would show considerable side effects. I'm not aware of any alternative treatments that would be nearly as effective as her current program.

Finally, G[redacted] has been able to cooperate with routine dental exams as part of period dental prophylaxsis. This is something that could not be done prior to institution of her aversive treatment program here at the JRC.

Edward Sassaman, M.D.

Exhibit 7

E[redacted] S[redacted]
DOB: [redacted]
DOA: [redacted]-2004

E[redacted] is a 17 ½ year old young woman with developmental delay and behavior problems. She's been a student at the school for almost four years. E[redacted] had been on numerous medications in the past including Zyprexa, Valproic Acid, Risperdol, and Artane. When she was admitted to the school, she was still on Zyprexa and Strattera. She did have abnormal liver function studies probably secondary to her psychotropic medications. These reverted to normal once she was taken off of medications. Her current medications are Albuterol, Benzoyl Peroxide, Hydracortisone, and Valisone. She has no allergies to any medicines.

E[redacted] currently is in excellent health. She was begun on aversive interventions in March 2006. These were for her health dangerous behaviors which included marked aggression towards, smearing feces, induced vomiting, and self-mutilation. Within one month of going on aversive interventions, these health dangerous behaviors decreased dramatically. She currently is in good health and making excellent progress. There is no question that she has experiences a substantial improvement in the quality of her life. She now is a classroom working towards her GED as part of an IEP program. She's able to go on regular community activities along with her class and her residence, and she's able to cooperate for all school and community well child and specialists health appointments, as well as dental appointments.

I'm unaware of any alternative treatments that would be effective with E[redacted] since she's been on most of them in the past and has had side effects from them as evidence by her abnormal live function studies. These treatments were ineffective in controlling her significant health dangerous behaviors. If she were not in a program such as the JRC, I seriously doubt that she would be able to participate in the community activities and be working towards her GED.

Edward Sassaman, M.D.

Exhibit 8

S[redacted] S[redacted]
Date of Admission: [redacted]-2005

S[redacted] is a 15 year old young girl with severe mental retardation, severe self-injurious behavior and numerous episodes of eye surgery with detached retina secondary to severe self-injurious behavior. S[redacted] has been a student at the school for almost three years. She was on numerous medications in the past including Fluoxetine, Naltraxone, Valproic Acid, Risperdol, Lorazapam, Prozac, Buspar, Tenex, and numerous combinations of eye drops. She currently is on no medications.

When she was admitted, she had abnormal liver function studies; probably secondary to several of her psychotropic medications. She had severe self-injurious behavior with health dangerous behavior consisting of rubbing her eyes and hitting her eyes with her knee. She had eye surgery at MA Eye & Ear Infirmary in April of 2005. The aversive procedures were started shortly there after and her health dangerous behavior consisting predominately of self-injurious behavior to her eyes decreased precipitously. Since that time, she has been able to continue to be followed at MA Eye & Ear Infirmary. Right now she is felt to be doing so well that she only needs to be followed yearly. In addition, the numerous eye drops that she had been on have been discontinued. Similarly, her dentition, which was in poor repair at time of admission, has improved considerably. She can now have periodic dental prophylaxsis. Her gingivitis, which was pronounced, is now quite stable.

There's no question that S[redacted]'s quality of life has improved dramatically because of the aversive interventions here at the JRC. She's made dramatic progress. I'm unaware of any alternative treatments that would be effective since all treatments had been tried previously. If the aversive treatments had not been used, I'm also convinced that S[redacted] probably would have had at least several more eye injuries and probable retinal detachments, and she very well might be blind by now. She suffered no harm as noted in the records from the aversive intervention. She currently is in excellent health.

Edward Sassaman, M.D.

Exhibit 9

H[redacted] S[redacted]
DOB: [redacted]
DOA: [redacted]-2005

[redacted] is an 11 ½ year old young man with multiple congenital anomalies, mental retardation, and severe self-injurious behavior. H[redacted]'s past history is significant for multiple congenital anomalies including a bicuspid aortic value and dilated ascending aorta. He also has a cleft palate. Because of his multiple congenital anomalies, H[redacted] required numerous appointments with health care providers in the past. Many of these appointments had to be cancelled because of his severe behavioral problems.

When H[redacted] arrived at the JRC, he was on Inderal and Risperdol. These were quickly discontinued. His alkaline phosphatase, a liver function study, was elevated on admission, but it quickly reverted to normal. H[redacted] had major problems with health dangerous behavior including severe self-injurious behavior and leaving a supervised area. His severe self-injurious behavior was such that he was unable to attend frequent medical appointments. He began GED in January 2006, and his health dangerous behaviors disappeared almost immediately. Since that time, he has been able to attend all school and community based appointments with health care providers. He needs to be followed by pediatric cardiology and ENT because of his cleft lip and palate. His father is thrilled with the progress that he's made and hopes that at some point the surgery for the congenital anomalies can be completed since it had to be suspended because of H[redacted]'s severe self-injurious behavior.

Overall, he is in excellent health now. The quality of his life has improved dramatically since he has been able to receive routine and specialty medical and dental care. In addition, he is able to participate in school and community activities. He suffered no side effects from the aversive program. I'm unaware of any alternative treatments that would be effect for H[redacted] besides the aversive program here at the JRC since all known treatments were attempted prior to his arriving here.

Edward Sassaman, M.D.

Exhibit 10

CURRICULUM VITAE

Edward A. Sassaman, M.D.
Excellus BlueCross BlueShield, Rochester Region
165 Court Street
Rochester, NY 14647
585-238-3653
ed.sassaman@excellus.com

EDUCATION

Undergraduate:	University of Pennsylvania Biology, BA 1969 – Cum Laude
Medical School:	Harvard Medical School – M.D. 1973

POSTGRADUATE TRAINING

Resident:	Children's Hospital Medical Center, Boston, MA Intern: 1973-1974 Junior Resident: 1974-1975 Senior Resident: 1975-1976
Fellowship:	Children's Hospital Medical Center, Boston, MA Development Evaluation Clinic Fellow in Development Disabilities: 1976-1978

BOARD CERTIFICATION AND PROFESSIONAL LICENSES

Diplomate, America Board of Pediatrics – 1978
Massachusetts – 1976 – Present
Rhode Island – 1978 – 1996
New York – 1994 - Present

PROFESSIONAL EXPERIENCE

2000 – Present

Excellus BlueCross BlueShield, Rochester Region
Rochester, NY
(A national indemnity and managed care health insurance company with revenues of over $4 Billion and 2.2 million covered lives.)
Regional Medical Director

Responsibilities: Responsible for developing and implementing managed care programs for children and adults throughout all of Excellus. Consultant for case management, utilization management, and corporate medical policy for all members.

Direct responsibility for overseeing all of provider credentialing and re-credentialing throughout all of Excellus and Univera. Reports to the Vice President of Medical Affairs and Chief Medical Officer of Excellus BlueCross BlueShield, Rochester Region.

Accomplishments:

- Implementation of community-wide Pediatric Preventive Health Guidelines
- Creation and implementation of disease state management program for Attention Deficit Disorder
- Common credentialing and re-credentialing policies (with specific guidelines for outliers created for all of Excellus and Univera)
- Established linkage between quality and credentialing (system to identify quality outliers and monitor QIP through credentialing)

1994 – 2000

Medical Director, Lifetime Health
Associate Corporate Medical Director, BlueCross BlueShield
Rochester, NY
(A mixed model HMO with 65,000 members and revenues of $82 million)

Responsibilities: Direct supervision of entire medical staff, including affiliated health professionals (125 FTEs). Direct responsibility for utilization management, quality management, case management, pharmacy benefit management, disease state management. Reported to the Vice President of Medical Affairs, BCBS Rochester.

Accomplishments:

- Oversaw doubling in size of medical staff
- Created and implemented disease state management programs in diabetes and congestive heart failure
- Created and implemented physician incentive program
- Created and implemented department and individual PCP quality and utilization yearly goals with method to revise goals based on department and individual performance
- Created peer review process to identify medical errors and create quality improvement process to rectify errors

1990 – 1994

Director of Pediatrics, Kaiser Permanente
Springfield, Massachusetts

Responsibilities: Direct supervision of pediatric staff responsible for quality issues. Practicing pediatrician. Reported to the Director of Pediatrics for Kaiser Permanente of Massachusetts.

Accomplishments:

- Oversaw doubling of pediatric department
- Implemented program for evaluation of handicapped children

1984 – 1990

Practicing Pediatrician
Medical West
Springfield, Massachusetts

Responsibilities: Providing primary care to 2,500 children

Accomplishments:

- Creation of consultative service for developmentally disabled children for a group of 12 practicing pediatricians

1978 – 1984

Associate Director, Child Development Center
Providence, Rhode Island
(A Federally and State-funded multi-disciplinary clinic for handicapped children)

Responsibilities: Direct supervision of pediatric staff and fellows as well as pediatric residents and medical students at Brown University Program in Medicine. Director of Muscular Dystrophy Clinic and Spina Bifida Clinic. Reported to Director, Child Development Center.

Accomplishments:

- Oversaw increase in teaching responsibilities with residents and medical students
- Created outreach program for community-based pediatricians

ACADEMIC/HOSPITAL APPOINTMENTS

1. Clinical Instructor in Pediatrics

   1994 - Present

   University of Rochester School of Medicine
   Rochester, NY
   Associate Attending Physician
   Strong Memorial Hospital
   Rochester, NY

2. Attending Physician — 1984 - 1994
   Baystate Medical Center
   Springfield, MA

3. Assistant Professor in Pediatrics — 1978 – 1984
   Brown University School of Medicine
   Providence, RI
   Associate Physician
   Rhode Island Hospital
   Providence, RI

4. Instructor in Pediatrics — 1977 - 1978
   Harvard Medical School
   Boston, MA

STATE OF NEW YORK APPOINTMENTS

Expert Reviewer in Pediatrics
Office of Professional Medical Conduct
New York Department of Health
Albany, NY

MEMBERSHIP IN SOCIETIES

Fellow, American Academy of Pediatrics

REARCH INTERESTS

1. Medical Peer Review – categorizing medical errors by physicians and determining antecedent predictive factors.

2. Determining which components of a Diabetes Disease State Management Program correlate best with a positive outcome.

COMMITTEES

1. Lifetime Health Quality Utilization Management Committee – 1994 – 2000
2. Lifetime Health Peer Review Committee – 1995 – 2000
3. Lifetime Health Pharmacy and Therapeutics Committee – 1994- 2000
4. Lifetime Health Medical Management Steering Committee – 1997 – 2000
5. BlueCross BlueShield of Rochester Managed Care Quality Committee – 1995 – present
6. BlueCross BlueShield of Rochester Managed Care Credentialing Committee – 1996 – present
7. Blue Cross/Association for Retarded Citizens/United Cerebral Palsy Task Force to create community based primary care program for developmentally disabled adults – 1998 – present

8. Preferred Care Peer Review Committee – 1998 – present

9. Preferred Care Clinical Quality Team – 1998 – 2000

PUBLICATIONS

1. Nelson, R.R., Sassaman, E.A., Jost J., and Topp, S.: Neurodevelopmental sequelae of Hemophilus influenza (HIB) meningitis. Pediatric. Res. 12:336, 1979

2. Sassaman, E.A., Mulick, J.: Sterilization and the Retarded Female. Pediatrics 66:650, 1980.

3. Sassaman, EA., Zartler, A., and Mulick, J.: Cognitive functioning in children with carbamyl phophate synthetase deficiency. Journal of Pediatric Psychology 6:171-7, 1981.

4. Gaines, R.F., Pueschel, S.M., Sassaman, E.A., and Driscoll, J.L.,: Effect of exercise on serum creatine kinase in carriers of Deuchenne muscular dystrophy. Journal of Medical Genetics 19:4-7, 1982.

5. Sassaman, EA., Zartler, A.,: Mental retardation and head growth abnormalities. Journal of Pediatric Psychology 7:149-156, 1982.

OTHER PUBLICATIONS

1. Sassaman, E., McEneaney, J. (Eds.) Transportation of the Handicapped Student. Providence: Rhode Island Department of Education Press, 1980.

2. Sassaman, E., Medical Aspects of Down Syndrome. In: Down Syndrome: New Perspective in Biomedicine in the Behavioral Sciences. Pueschel, S.M. and Rynders, J.E. (eds.) New York: Garland Press, 1981

3. Sassaman, E., Siber, M., and Canal, T.: An evaluation of any early interventive program for children with Down Syndrome. In: A Study of the Young Child with Down Syndrome, Pueschel, S.M. (Ed.) New York: Human Sciences Press, 1983.

4. Sassaman, E.: Ethical considerations in medical treatment of the mentally retarded. In: Comprehensive Handbook of Mental Retardation, Matson, J.L. and Mulick, J. (eds.) New York: Pergamon Press, 1982.

5. Sassaman, E.: The parent-physician teams. In: The Parent-Professional Decision Making Process in Developmental Disability Services. Pueschel, S.M. and Mulik, J. (eds.) Cambridge: The Ware Press, 1983.

6. Mulick, J., Sassaman, E.: Encyclopedia of Pediatric Psychology by Logan Wright, et al. Book Review, Journal of Autism and Developmental Disabilities 10:108, 1980.

7. Sassaman, E.: The Practical Management of the Developmentally Disabled Child by Albert Scheiner and Israel Abrams. Book Review. New England Journal of Medicine 304:548, 1981.

8. Zartler, A., Sassaman, E.: Linguistic development in phenylketonuria (letter to the editor). Journal of Pediatrics 99:501, 1981.

9. Sassaman, E.: The Mildly Handicapped Student by Ted Miller and Earl Davis. Book Review. New England Journal of Medicine 307: 1535, 1982.

10. Sassaman, E.: Autism in Adolescents and Adults by Eric Scholper and Gary Mesibov; Autistic Children: New Hope for a Cure by Niko and Elisabeth Tinbergen. Book Review. New England Journal of Medicine, 309:675, 1983.

11. Sassaman, E.: No Fault Parenting by Helen Neville and Mona Hulaby. Book Review. New England Journal of Medicine, 317:285, 1985.

12. Sassaman, E.: Sudden Infant Death Syndrome. In: Under Three. O'Shea, J. (Ed.) New York: Von Nostrand, Rhineholt, 1988.

13. Sassaman, W., Sassaman, E.: Twins. In: Under Three. O'Shea, J. (Ed.) New York: Von Nostrand, Rhineholt, 1988.

14. Sassaman, E.: Tests and Procedures In The Special Child. Pueschel, S. (Ed.) Baltimore: Paul H. Brooks Publishing, 1988.

EXHIBIT 22

FUNCTIONAL BEHAVIORAL ASSESSMENT

Student: D[redacted] B[redacted] **Prepared by: Patricia Egan, Ph.D., BCBA**
DOB: [redacted]94 (9.5 yrs.)

Historical Patterns and Current Behavior

D[redacted] has experienced extended periods of time (i.e., up to six months) in which he demonstrates the ability to: (a) follow school rules and instructions from adults; (b) participate successfully in individualized and inclusive educational sessions; and (c) socialize with adults and sometimes peers. During these times, he responds well to individual accommodations, such as personal schedules, break passes, and a token system.

In the last two years, however, D[redacted] has intermittently experienced episodes of behavioral regression so disruptive that he has needed to be instructed in a quiet area away from his classroom and, thus, isolated from his peers. The episodes have included the following behaviors: screaming, aggression (hitting, kicking, scratching, pushing, spitting at others), running away, and property destruction. When episodes occur, D[redacted] does not comply with adult directives to stop the behavior. The isolated area in which he has worked (*planning area*) is an open storage and copy room frequented by staff and it also serves as a passageway to the offices of school counselors. The room also has a closed door time out room. At times when D[redacted]'s behavior has been dangerous, he has been physically escorted by staff to the time out room, where he has remained until quiet.

In the planning area, with complete one-to-one staff attention, decreased academic demands, choices of tasks and activities, and increased positive reinforcement, D[redacted] has usually been more receptive to staff interactions and more compliant with school rules. He returns to the classroom as soon as his disruptive behavior ends, usually within 30 minutes. Academic and social demands are then gradually increased and tangible reinforcers are gradually faded to more natural levels. When staff make the determination that his behavior is dangerous, his father has been called to pick him up from school early, and D[redacted] has returned to school the following day without problems.

At times, however (approximately once or twice per year), D[redacted]'s severe disruptive behavioral episodes occur at such continuous rates that he has needed one-to-one instruction in the planning area for up to several consecutive days. These behavioral regressions have occurred approximately once or twice per year, and they have occurred without noticeable environmental changes (e.g., of staff, schedule, structure, etc.). During these regressions, D[redacted] refuses most tasks and activities; and he engages in negative verbal responses such as threats to hurt people, requests to go home, and noncompliance. These behaviors then escalate to more physically dangerous behavior, such as knocking over furniture, running away, and physical aggression to staff. When

these behaviors reach a level that the staff consider dangerous, D[redacted]'s father is called and he is asked to pick D[redacted] up from school because of the risk of injury to staff, other students, or D[redacted].

Functional Behavioral Assessment Methods

For the past two years, D[redacted]'s behavioral episodes are documented on a coded scatterplot data sheet that provides ongoing functional assessment interval data, via direct observation. Additionally, D[redacted]'s father and his classroom staff are frequently interviewed to discern setting events and environmental variables that precede or interact with disruptive behavioral episodes. Data collection and evaluation methods have been supervised by Dr. Patricia Egan, a Certified Behavior Analyst and NYS School Psychologist who specializes in behavioral programs for children with autism spectrum disorders.

Functional Behavioral Assessment Summary Statement (results of direct observation, interviews, and environmental manipulations)

There are times when D[redacted] attempts to escape or avoid the social and academic demands of school by engaging in severe disruptive behavior. Disruptive behaviors include: noncompliance to directions, screaming, hitting, kicking, scratching, spitting, property destruction, running away, and verbal threats. Sometimes the rate and intensity of his disruptive behaviors increases when: (a) demands are placed on D[redacted]; (b) reprimands or an angry, dictating tone of voice is used; or (c) his requests for preferred activities are denied. They also escalate when physical intervention is used. Physical intervention has been necessary, however, to interrupt potentially dangerous behavior (climbing on furniture, running away, property destruction, physical aggression to others) when D[redacted] is noncompliant to verbal instructions to stop.

It should also be noted here that, in response to his recent increase in disruptive behaviors, D[redacted] has experienced several medication changes over the past six months. The medication changes have sometimes occurred in conjunction with changes in behavioral intervention methods, making it more difficult to discern the effects of behavioral or pharmacological interventions.

POSITIVE BEHAVIORAL SUPPORT PLAN

Name: D[redacted] B[redacted]	**Behavior:** Disruptive episodes
Type of FBA: Direct observation; antecedent manipulations; staff, student, parent interviews.	**Hypothesis:** Escape/aoidance; tangible
Definition: Noncompliance paired with any of the following: screaming, hitting, kicking, scratching, spitting, verbal threats, running away, or property destruction.	
Measurement System: Interval record of specific behaviors, frequency and duration of time out.	
Baseline Procedure:	
Objective: Damian will exhibit no more than one disruptive episode per month across 6 consecutive months.	

PROGRAM DESCRIPTION

Plan 1

Prevention Techniques: Use time timer for tasks and activities. Have his personal schedule available each day. Provide the option for him to work in a quiet place in the classroom (use partitions). Integrate preferred activities and tasks with more challenging and less preferred activities and tasks. Reduce inclusion in general education and special education classes as needed to decrease anxiety and avoid problem behavior. Minimize talking, and monitor voice and body language to avoid negative or dictating tone/style. Reduce demands after lunch and at other times when D[redacted] seems restless or unsettled.

Reinforcement Plan: Reinforce absence of disruptive behavior with stickers and D[redacted]'s choice of backup reinforcer (e.g., computer, library, music, bike, etc.) after three stickers. Use continuous schedules of reinforcement via stickers at high-risk times, and increase criteria (intervals up to 15 min.) as his behavior improves. Also reinforce polite speech. Constant praise throughout the day for good work, appropriate behavior, etc..

Adaptive Alternatives: Break passes should be available at all times. Observe constantly for signs of agitation and prompt D[redacted] to take a break when needed. Rehearse the rules and how to ask for help before every transition. Use model prompts to teach him to ask for clarification or to express confusion. Reward polite interactions with stickers.

Immediate Consequences: For noncompliance to instruction or minor episodes of target behavior, instruct D[redacted] to take a break. If no response to verbal direction, remove attention and leave D[redacted]'s area. If he stops the behavior, immediately turn attention back to him and praise the first appropriate response he makes. If he refuses to comply and continues to engage in disruptive behavior, physically escort him to the time out room and follow Plan 2.

Notify parents of D[redacted]'s behavior daily, via notebook.

PROGRAM DESCRIPTION

Plan 2

Prevention Techniques: D[redacted] works at a desk in the planning area, with two staff available. One staff person is designated as D[redacted]'s instructor, and another adult is available nearby, to help with physical intervention and other support as needed. Staff rotate approximately every 30- to 60-minutes. Use time timer for tasks and activities. Personal schedule available each day. Break passes available at all times. Encourage him to take a break when needed. Work only on less demanding tasks and activities. Provide visual forced choices (i.e. choice of two tasks) of activities and then help get him started. Terminate inclusion in general education classes temporarily, and specials as needed for safety. Monitor voice and body language to avoid negative or dictating tone/style.

Reinforcement Plan: Reinforce absence of disruptive behavior with stickers and D[redacted]'s choice of backup reinforcer (e.g., computer, library, music, bike, etc.) after three stickers. Also reinforce polite speech. Constant praise throughout the day for good work, appropriate behavior, etc.

Adaptive Alternatives: Break passes should be available at all times. Observe constantly for signs of agitation and prompt D[redacted] to take a break when needed. Rehearse the rules and how to ask for help before every transition. Use model prompts to teach him to ask for clarification or to express confusion. Reward polite interactions with stickers.

Immediate Consequences: When D[redacted] begins a verbal threat, property destruction or potentially dangerous behavior, prompt him to stop with a warning about time out (i.e., "D[redacted], you need to come down from there, or go to time out"). If he refuses, immediately escort D[redacted] to the time out room. Monitor constantly. After 30 quiet seconds (no disruptive behavior; sitting or standing in one place), open door and say "okay, you can come out whenever you're ready" and allow D[redacted] to remain in the open door time out room for as long as he needs to. When he exits time out, direct him to sit in a chair next to the time out room ("cool-down chair"). If he begins disruptive behavior in the cool-down chair, remind him of the rules: hands to self, follow directions, and stay in seat. If he violates the rules, return him to the time out room. Minimize interactions while in the cool-down chair, but talk with him briefly and/or give him simple instructions to follow to assess his ability to return to his desk. Invite him to return to his desk after 30 quiet seconds. If he refuses, wait another 30 seconds and repeat invitation. Continue until he returns to work and begins earning stickers again.

Notify parents of D[redacted]'s behavior daily, via notebook or through direct communication.

Consent for Use of Environmental Time Out

Student: D[redacted] B[redacted]
DOB: [redacted]94

Environmental time out will be used only as a necessary and last resort for the protection of students or property. The attached Positive Behavioral Support Plan (Plan 2) describes positive procedures that will be implemented to avoid the use of time out. Staff will use time out procedures as described in the plan, and will escort D[redacted] to the time out room as needed using the least intrusive and most effective physical intervention methods possible. D[redacted] will be visually monitored constantly while in the time out room (observed at least every 10 seconds). Time out durations will be only as long as necessary for D[redacted] to regain control of himself (see Plan 2). Any incident which requires the use of environmental time out will be documented on a data sheet, along with the duration of the time out. Further description information of the incident(s) will be documented in an incident report at the end of the day. Parents will be notified of any incidents that occur. Data will be evaluated at least weekly by a certified behavior analyst and psychologist, Patricia Egan, Ph.D..

Potential Risks
Potential risks of the program described in the attached plan include:

- The risk of injury to D[redacted], staff, or other students, especially during physical escort to the time out room;
- Disruptive behavior may occur in the time out room;
- The procedures may not be effective in decreasing D[redacted]'s rate or intensity of disruptive behavior.

I have read this consent form and the descriptive information attached. The program was explained to me in understandable terms. I give my informed consent to the Franklin-Essex-Hamilton BOCES staff to follow the prescribed procedures. I understand, however, that I may withdraw my consent at any time.

Parent	Date
Franklin-Essex-Hamilton BOCES Administrator	Date
Behavioral Analyst/Psychologist	Date

EXHIBIT 23

MATRIX HEALTH SYSTEMS

PSYCHIATRIC CONSULTATION

M. DIANE ZUNIGA, MD

Patient: D[redacted] B[redacted]
DOB: [redacted], 1994
Parents: R[redacted] B[redacted] and C[redacted] B[redacted]
School: Petrova (BOCES)
Grade: First
Physician: Dr. George Cook
Date of the Evaluation: April 26, 2002

Sources of information:
An interview with D[redacted], his mother R[redacted] B[redacted] and C[redacted] B[redacted] as well as review of the following information:

- Pediatric Developmental Evaluation dated September 13, 1999.
- Annual speech and language progress notes and objectives.
- Occupational therapy progress note dated June 2001.
- School behavioral interventions and disciplinary referrals dated September 11 2001 through January 15, 2002.
- IEP for the 2001/2002 school year.

Reason for evaluation:
The mother indicated she was very concerned as D[redacted] is approximately seven and a half years of age and he is functioning at a two and a half to three year old level. He likes Barney and Blues Clues rather than age appropriate movies and activities. They report his only motivation is a cookie. He does not want to leave the home and only wants to play outside the house or wants to remain inside watching TV. They report that he has tantrums when he does not get his way. They described an episode in which he had a tantrum in the middle of a busy road as he was not allowed to get down on his hands and knees to follow the yellow line with his hands. They report he is asleep by 9:30PM and sleeps well. He is awake by 7:00AM without any difficulty. They report a good energy level. He is a very picky eater. He will eat bananas, yogurt, breads or pasta but generally will eat no meat or vegetables. He will also refuse milk. They describe his mood as mostly "happy go lucky". They reported that aggression was not a problem but then were able to admit that he does hit the mother and occasionally will hit the father. Review of records indicate numerous episodes of aggression towards the staff including hitting, biting, kicking, spitting etc. They state he knows when things are out of place. Every day he will ask in an almost ritualized manner why the cat is standing at the feeding mat. He is reported to interact very little with peers at school although he is now mentioning peers names even when he is at home. He prefers to interact with adults and older children. He will insist at times that people will call him other than his name of D[redacted]. He will insist

on names such as "Officer D[redacted]" or "Rover". He frequently will act like a dog and that is the parent's clue to call him Rover. During his temper tantrums he will stomp his feet and scream. They report that stores are very difficult as he will tantrum if they do not have a cookie or any other samples to give him. Tantrums usually last only a few minutes but he can have none in a week or as many as ten in a day. He will stop if he is promised cookies or promised to be allowed to watch a favorite program. He will frequently mix up genders and will call his mom "sir". He will perseverate for a few hours on different objects, such as a broken object or the cones on a work truck. He appears to be very fascinated about specific things, which he will then perseverate on. He enjoys whirling in circles and will flap his arms when upset. At times he will use phrases that he has heard other people use and will use the phrases with his parents such as calling his parents "young man". He will also call them "stupid, peanut head or loser". He enjoys taking things apart, in fact he likes to see things broken in order that he can see them fixed. He plays with Lincoln logs and uses them as a hammer rather than building. The parents describe him as a helper. The parents indicate that he has always made good eye contact with them however, it is reported differently at school. The parents do admit that he tends to remain in his own little world and tends to control everyone around him. He enjoys being held on someone's lap and enjoys being near people but does not want the parents to put their arms around him and hug him. The mother describes an incident recently in which he tantrumed because she would not allow him to drive her car.

Past Psychiatric History:

He was noted to have problems at three years of age. He was referred in September 1999 to Dr. Debra Kriss who diagnosed him with Pervasive Developmental Disorder NOS. No recommendations were made for medication at that time however, supportive therapies were recommended. He did receive play therapy in Kindergarten from Jennifer Tissot. He is currently being seen by Brian Betastoni as well as Dr. Patricia Egan a behavioral psychologist who has written behavioral plans for him.

Family Psychiatric History:

D[redacted] is the son of R[redacted] and C[redacted] B[redacted]. R[redacted] B[redacted] is thirty-five years of age and in good physical health. She is a bus driver and a classroom aide. She is the oldest of four children. Her parents divorced when she was six years of age and her mother remarried. Her stepfather adopted all the children. She states that she did locate her birth father when she was sixteen years of age. She states that her father admitted to having problems with substance abuse and in fact when she visited him his license had been revoked for a DWI. She has two years of college and reports no behavioral or academic problems. Her own mother was adopted and she knows little of her father's family. R[redacted]'s brother has problems with depression. Otherwise R[redacted] denies any family psychiatric history. C[redacted] B[redacted] is fifty-four years of age and in good health. He is a merchant. He was the older of two children and has a Bachelors Degree. He denies any behavioral or academic problems. He remembers stuttering in third grade. But otherwise denies any psychiatric history in himself or in his family.

Social History:
R[redacted] and C[redacted] B[redacted] were together for twelve years. They have two children, J[redacted] who is twelve years of age and D[redacted] who is seven and a half. They report J[redacted] is bright and alert and is very mature for his age. They were separated on April 18, 2001 and their divorce was finalized on January 31, 2002. They deny any physical abuse they state that they are able to interact well with regards to the children. The father has legal custody and the mother has unlimited visitation. They generally have alternate weekends and the mother will stop by every night to visit. They currently live in Saranac Lake. The mother has a significant other who the children get along with.

Developmental History:
It was a planned pregnancy. The mother smoked half to one pack per day throughout the pregnancy. She denies any other drug use or complications. It was a full term spontaneous vaginal delivery. He was ten days overdue. Birth weight was nine pounds, two and a half ounces. She was able to nurse him for the first few months and then he was bottle-fed. She describes him as unusually calm and was able to sleep through the night immediately. He was a very easy baby. The mother was able to stay home with him for the first six years. His first words were not said clearly until he was about three and a half years of age. He would usually scream when he wanted something. He was walking at twenty-two months. At three years of age review of notes indicate that he was not toilet trained and was basically non-verbal. He was unresponsive to most directives from adults and had frequent tantrums. At four years, nine months he was using jargon speech with echolalia and required visual cues to understand what was going on. Decreased eye contact and indiscriminate friendliness was noted. He was toilet trained between three and a half and four years of age however, he continues to be enuretic at night.

Medical History:
He has always been described as very healthy. His physician is Dr. George Cook.

Educational History:
He began pre-school at three years of age for two days per week. At that point the teacher expressed concerns. In October 1998 he attended Children's Corner during that time he received a physical therapy briefly but began receiving speech and occupational therapy regularly. He attended BOCES pre-school at Lake Colby at five years of age. Last year he was mainstreamed to Kindergarten at Lake Colby and in the afternoons received special education with Terry Smith. They eventually switched to a full day of special education with Terry Smith. He has always had a one-to-one aide throughout his schooling. He is currently attending first grade at Petrova and in a 6:1:1 program. He is reported to have difficulty with transitions. He was suspended from school in November 2001. The parents report that this was because he was "screaming in the time out room". They also reported that he was written up for having some problems on the bus. Review of school reports indicate that he was having significant and numerous problems with aggression. Most of these episodes appear to be related to transitions. At other times he would attempt to hide in back of a shelf or to lock himself in the closet. He was also running from staff. Other episodes would occur when he did not want to comply with an

adult request. The parents report that he is now enjoying school more as they believe the school is currently working more with him. An IEP is planned fairly soon. At six years, six months he was administered a ROWPVT. He scored a standard score of eighty-one which placed him in the tenth percentile functioning at the four year nine month for receptive vocabulary.

Mental Status Exam:

This is a good-looking blonde boy with rosy cheeks. He is well nourished with good hygiene and casual dress. He was noted to exhibit much physical contact with his father and at times would sit on his lap and put his face very close to his father's face and rub noses with him. He was noted to make more contact with his father than with his mother. At other times he would scratch the arms of his parents in what appeared to be an affectionate manner. Throughout the session he spoke very little. He was noted to pretend to be a dog and would make barking sounds and almost claw like a cat. At other times he would be found under the table or sitting quietly on a large stuffed bear in the corner. He had much difficulty separating with his father and in fact refused to separate from him. The father was allowed to stay in the room at which point we did most of the interview. The father did leave after a period of time and he was able to remain in the room with me however, throughout that time he would continue to play and state almost casually "Where's dad? I miss him". While his father was gone he spent the entire time playing with his back to me. He was able to repeat three out of three objects immediately. When asked to repeat them after ten minutes he could not do so however, when I prompted him with the first word he could remember the other two objects. When asked to name his teacher he pointed to his dad and stated "you a teacher". Even with the father trying to assist him with naming the teacher he eventually stated "Lorraine" however, the father states this was not correct. He was very difficult to engage and in fact would frequently not respond to many of my questions. At other times he would interrupt and say out of context "a broken chair". He would also pretend to sleep and would snore loudly. When asked to count the bears around the tea set he stated there were four, when actually there were three bears and one boy doll. He was noted to mumble to himself while playing with the tea set however; his mumblings consisted of various unrelated objects such as "chair, people, house, etc". He was able to identify that one of the bears was red. He was noted to be somewhat clumsy in handling the objects. At one point he dropped a cup and demonstrated a very frightened look on his face. He did calm easily. Articulation appeared to be mostly fair, although he did exhibit an inappropriate use of pronouns. At times he would appear to have an almost sing song voice. He was very controlling in his play. When I asked him for some tea he responded "no". He then pretended to serve me tea and pretended to throw the contents of the cup at me. Rather than playing with the tea in a usual manner, he stacked up the plates and the cups and attempted to balance them on his head or on the bear's head. When I asked if the bears were going to get tea he responded with "no, tea time is over".

Diagnosis:

Axis I: Aspergers
Nocturnal Enuresis

Axis II:	Deferred
Axis III:	None
Axis IV:	Parental divorce
	School and social difficulties
Axis V:	30

Recommendations:

The diagnosis of Aspergers was discussed with the parents. The parents appeared to have some difficulty understanding and accepting the diagnosis and tended to minimize some of his symptoms especially that of aggression. It was explained to them that there was not a medication that would cause D[redacted] to function at a normal level and that this would be a very slow process for him to catch up and that this might not even happen until adulthood. Even in adulthood he will most likely continue with some odd or eccentric behaviors. It is important that the family and the school be educated as much as possible on this disorder. Paperwork was given to the mother in helping her to address different behavioral problems seen in Aspergers. We also discussed the fact that he tends to be very controlling, which is probable due to his underlying anxiety and confusion with societies norms and expectations. A trial of Zoloft is recommended beginning at 12.5 mg q/am. We discussed different side effects with the most common being difficulty falling asleep at night or possibly even drowsiness, jitteriness or stomach upset. These symptoms should resolve. Children with Aspergers tend to respond to very small doses of Zoloft. Should he have no response after three weeks, I would then consider increasing his Zoloft to 25mg, this can be titrated slowly as needed to respond to controlling behaviors. He appears to have much difficulty with transitions. Behavioral programs will need to be instituted so he is aware of his schedule. Some children have resounded well to red light, yellow light and green light. Yellow light being that they will soon be transitioning to the next scheduled activity and the red being to stop the current activity, green light being to begin the next activity. It is also recommended that a teacher's and parent's Connors be obtained in order to obtain a more objective measure of his hyperactivity and impulsivity. It is not uncommon for children with Aspergers to have ADHD symptoms, Obsessive Compulsive Symptoms, anxiety and aggressive outbursts. Children with Aspergers are treated symptomatically depending on the symptoms they present with. Family members will require much support and ongoing counseling. It is important that there be consistency between the two homes and school as far as setting limits and working together as he will respond better to consistency in all three areas. The parents have agreed to do so.

Thank you for this referral.

M. Diane Zuniga MD

M. Diane Zuniga, MD
Psychiatrist
Child and Adolescent Board Certified

EXHIBIT 24

CHAMPLAIN VALLEY PHYSICIANS HOSPITAL MEDICAL CENTER
Plattsburgh, New York

HISTORY AND PHYSICAL

PATIENT NAME: B[redacted], D[redacted]

DOB: [redacted]1994 AGE: 9
MEDICAL RECORD#: [redacted]

ADMISSION DATE: [redacted]/2004

ATTENDING PHYSICIAN: Diane Zuniga, MD

HISTORY OF PRESENT ILLNESS
The patient is a 9-year-old currently followed by Dr. Van Dyck as an outpatient. He was seen by AMC on May 11th and hospitalization was recommended for him. Father refused. He was taken for an outpatient appointment on May 14th to see Sally Gilpin, CSW. At that time, the patient attempted to leave the office. When the therapist attempted to keep him from doing so, he became extremely aggressive and out of control. Father had difficulty setting limits. Father did not want hospitalization and felt that the patient only needed to be sedated and that he could handle him at home as long as he was not told the word no. CPS became involved. As father refused inpatient hospitalization, CPS took custody. He was admitted overnight to Adirondack Medical Center until he was referred here. At Adirondack Medical Center, he was aggressive and out of control even with police officers. He received p.r.n.'s of droperidol 2.5 mg and Ativan 1 mg IM. He continued to be very fidgety and restless and required soft restraints. Reportedly, the patient has normal sleeping and eating patterns. He likes watching commercials about cereal characters. He can be aggressive towards anyone especially when told no.

PAST PSYCHIATRIC HISTORY
The patient has been diagnosed with pervasive developmental disorder. He has been treated as an outpatient by Dr. VanDyck. He is most currently on Paxil CR 25 mg per day and Seroquel 125 mg per day. Review of records indicates he has been on Zoloft in the past. This was discontinued in January of 2004. He was also on Risperdal in the past, which was also discontinued.

FAMILY PSYCHIATRIC HISTORY
The child is the son of C[redacted] B[redacted] and R[redacted] B[redacted]. I was unable to reach them by phone. Review of records indicates that mother has a history of anorexia and bulimia. She is currently living with D[redacted] R[redacted] There are reported to be fights and abuse, alcohol and drugs. The patient is currently under the care of his father. There is no other family psychiatric history available at this time. There is no developmental history available.

SOCIAL HISTORY
The patient also lives with his 14-year-old brother. The patient is currently in the third grade _____ School, BOCES program. He has been become increasingly aggressive and out of control. He has been having to be picked up by his father from school anywhere from three to four times per week and was suspended from school in the last month. Patricia Eagan is the school systems behavioral therapist. Sandy Thomas-Kirsch is the advocate at Watertown Learning Association. The patient is now currently under the care of Franklin County Department of Social Services.

MEDICAL HISTORY
His physician is Dr. Cook. No known health problems. There is no other medical history available at this time.

PHYSICAL EXAMINATION
Height 5'4", weight 33.1 kilograms. Temperature 98.7, pulse 114, blood pressure 110/80, respirations 14.

The patient refused a physical exam. He was extremely hyperactive and was running all around the room. He did not respond to verbal re-directions. Only parts of the physical were obtained as able.

The lungs were clear to auscultation.

Heart rate was rapid but of regular rhythm.

He did appear to have bowel sounds.

He was ambulate without difficulty.

MENTAL STATUS
The patient was alert. He did not make eye contact. He was extremely hyperkinetic. He was not cooperative, was very inpatient. He was not appropriate and was labile. When restrained in any way from doing something, he would become very loud and would yell, "you are lying, you are a liar." He would repeat, "When am I going home?" He was not responsive to redirection. He could be loud at times. He would spontaneously ask when he was going home. He did not appear to comprehend the response because he would ask the question again. He appeared to be very concrete. His attention span was poor. He has no insight. His impulse control and judgment are very poor.

ASSESSMENT

AXIS I: Pervasive Developmental Disorder, rule out ADHD combined. Rule out Mood Disorder.

AXIS II: Deferred.

AXIS III: None known.

AXIS IV: Separation of parents, poor school performance, lack of limit setting and structure in the home.

AXIS V: 30.

PLAN

The patient is noted to be extremely hyperactive. I will give a trial of Tenex and I will attempt to taper and discontinue his other medications, possibly give him a trial of a stimulant and a mood stabilizer. Will need to contact Dr. Cook and Dr. Van Dyck for past medication trials. I will also need to contact the family for additional information. We will also need to contact ARC for help in setting limits and structure in the home.

Diane Zuniga MD
Diane Zuniga, MD

DZ:tfb
DD: 05/16/2004 3:03 P
DT: 05/16/2004 3:37 P
Job #: 000081218
Document #: 576877

cc: George Cook, MD
Diane Zuniga, MD

EXHIBIT 25

THE STATE EDUCATION DEPARTMENT / THE UNIVERSITY OF THE STATE OF NEW YORK / ALBANY, NY 12234

OFFICE OF VOCATIONAL AND EDUCATIONAL SERVICES FOR INDIVIDUALS WITH DISABILITIES
COORDINATOR SPECIAL EDUCATION POLICY AND PROFESSIONAL DEVELOPMENT
Room 1624 One Commerce Plaza • Albany, NY 12234 Telephone: (518) 486-7462 Fax: (518) 402-3583
www.vesid.nysed.gov

July 2, 2009

Mr. Chad McCarthy
CSE Chairperson
Saranac Lake Central School District
79 Canaras Avenue
Saranac Lake, NY 12983-1560

Dear Mr. McCarthy:

This is in response to the "Application to the Commissioner of Education for the Child-Specific Exception to Recommend Aversive Behavioral Interventions" submitted by the Saranac Lake Central School for D[redacted] B[redacted], a student attending the Judge Rotenberg Educational Center (JRC). The cover letter accompanying this application is dated February 2009; however the application was not mailed until June 25, 2009 and was received by the State Education Department (SED) on June 29, 2009.

Section 200.22(e) of Regulations of the Commissioner of Education provides that "a child-specific exception to the prohibition of the use of aversive interventions set forth in section 19.5 of this Title may be granted for a school-age student ... only during the 2006-2007, 2007-2008 and 2008-2009 school years; provided that a student whose IEP includes the use of aversive interventions as of June 30, 2009 may be granted a child-specific exception in each subsequent school year, unless the IEP is revised to no longer include such exception." A full text of the regulations may be found at http://www.vesid.nysed.gov/special ed/behavioral/finalamend.htm.

The Regents prohibition on the use of aversive interventions would, therefore, apply to D[redacted] because his IEP as of June 30, 2009 did not include a recommendation for the use of aversive interventions and because he had not received an exception to the prohibition of the use of aversive interventions during the 2008-09 school year. I am, therefore, returning D[redacted]'s application to you. If you have any questions, please contact Charlene Gurian at 518-486-7462.

Sincerely,

Patricia J. Geary

Patricia J. Geary

Enclosure
c: Charlene Gurian
Andrew Jackowski

EXHIBIT 26

The Devereux Foundation

Arizona
California
Connecticut
Delaware
Florida
Georgia
Maryland
Massachusetts
New Jersey
New York
Pennsylvania
Texas

December 19, 2008

Ms. Anne Kner, Social Worker and CSE Chair
District 21 (Brooklyn) NYC Department of Education
415 89th St.
Brooklyn, NY 11209

Re: S[redacted] T[redacted]
DOB: [redacted]
NYC ID#: [redacted]

Dear Ms. Kner:

I regret to inform you that the Devereux Foundation in Red Hook, New York can no longer serve and appropriately care for S[redacted] T[redacted], a student the NYC Board of Ed. has placed in our school. Due to the numerous self-injurious behaviors of multiple and continued teeth pulling, the frequency of attempts to try to manipulate his teeth, and the severity of this behavior in regards to his health, the treatment team of S[redacted] T[redacted] has made the decision that an alternate placement is necessary to properly care and program for this student. After speaking with the treatment team, the decision of not being able to serve S[redacted] has been made in conjunction with the school's Clinical Director, Dr. Ajit Doolabh, the school's Quality Director, Kelly O'Shaughnessy, and the National Coordinator for Neurodevelopmental Disorders, Dr. Vince Winterling.

According to dental intake information, S[redacted] was admitted on [redacted]/08 to the Devereux Foundation missing three teeth. While in the Devereux Foundation's care, S[redacted] has removed his teeth on four occasions: On 10/20/08, S[redacted] removed 2 teeth; on 10/29/08 he removed 1 tooth; on 11/18/08 he removed 1 tooth, and finally on 12/16/08, S[redacted] removed 1 tooth, despite our providing one to one coverage on a 24/7 basis for the prior several weeks. S[redacted]'s parents, G[redacted] and J[redacted] T[redacted] also state that while on a weekend home visit, on 10/19/08, he removed one tooth. On all occasions, the T[redacted] were notified by his case manager, Joseph Lansang. Mr. Lansang has also contacted your department regarding these incidents contemporaneously within the timeframe they have occurred.

As one can see, the severity of this behavior calls for an extremely high level of care. Your district is currently funding for a 1:1 staff for S[redacted] during all waking hours of each day. Due to the critical need for constant monitoring, The Devereux Foundation had put in place a 1:1 staff for S[redacted] T[redacted] during the overnight shift as well starting on 12/3/08; yet even with this staffing, S[redacted] still displayed this dangerous behavior and continues to manipulate and reach for his teeth.

In conclusion, this self-injurious behavior calls for a more restrictive environment, one in which we can not provide. As mentioned above, the Devereux Foundation in Red Hook, New York can no longer serve and appropriately care for S[redacted] T[redacted] we therefore are asking for the district to seek alternate placement as soon as possible, but believe he is vulnerable to continue this behavior while here. We will continue to serve S[redacted] until an appropriate placement is found, but urge your immediate attention. The case manager has informed S[redacted]'s parents of our decision of being unable to serve their son.

As always, we appreciate the opportunity to assist in the education of students in your school district and are saddened that this case has turned out the way that it has.

Regretfully,

John O'Keefe
Executive Director, Devereux Foundation

cc: Dr. Ajit Doolabh, Director of Clinical Services, Devereux Foundation
Mr. John Lopez, Principal, Devereux Foundation
Ms. Amelia Williams, Director of Residential Services, Devereux Foundation
Mr. Joseph Lansang, Case Manager, Devereux Foundation
Student File

EXHIBIT 27

The Devereux Foundation

Arizona
California
Connecticut
Delaware
Florida
Georgia
Maryland
Massachusetts
New Jersey
New York
Pennsylvania
Texas

December 22, 2008

Re: S[redacted] T[redacted]
D.O.B: [redacted]

To Whom It May Concern,

In my professional opinion, S[redacted] T[redacted] requires a more structured/restrictive environment than offered here at the Devereux Foundation, in order to control self injurious behaviors.

Sincerely,

B. Schutzman M.D.
Medical Director/Psychiatrist

40 Devereux Way, Red Hook, New York 12571
(845) 758-1899 Fax (845) 758-1817

EXHIBIT 28

The Devereux Foundation

Arizona
California
Connecticut
Delaware
Florida
Georgia
Maryland
Massachusetts
New Jersey
New York
Pennsylvania
Texas

ACKNOWLEDGEMENT & RELEASE

We, J[redacted] and G[redacted] T[redacted], parents and guardians of S[redacted] T[redacted], DOB [redacted] acknowledge that the clinical staff at The Devereux Foundation's New York Red Hook Campus School have informed us that despite every clinical intervention employed to date, including, but not limited to, 24 hour 1:1 supervision, that S[redacted] continues to engage in self injurious behavior. We further acknowledge that because of the severity of S[redacted]s ongoing behaviors that the Campus School clinical staff has recommended to us that S[redacted] be placed in a more restrictive treatment setting that can better address S[redacted]'s treatment needs. Despite our full awareness of these circumstances and recommendation, we have chosen to keep S[redacted] in treatment at Campus School.

Consequently, as long as S[redacted] remains in care at Campus School, his clinical team will continue to therapeutically address and clinically intervene in an effort to prevent or lessen his self-injurious behaviors, although the recommendation for a transition to a higher level of care continues. We agree that if S[redacted] causes bodily injury, other damages, including property damage, to himself or another as a result of his behaviors while at the school at Red Hook, that we will indemnify and hold The Devereux Foundation, its officers, directors, employees, agents and contractors harmless from any liability, cost, damage, settlement, judgment or other related expense.

We also agree that any medical expense incurred for treatment of any injury S[redacted] inflicts upon himself or another is not the responsibility of The Devereux Foundation.

Our signatures below demonstrate our agreement with the above and we acknowledge that our agreement was given freely and voluntarily.

Signed: _____
J[redacted] T[redacted] (mother)

Print Name: _____

Date: _____

Signed: _____
G[redacted] T[redacted] (father)

Print Name: _____

Date: _____

40 Devereux Way, Red Hook, New York 12571
(845) 758-1899 Fax (845) 758-1817

EXHIBIT 29

Children's Hospital Event Notification System
NOTIFICATION OF ADMISSION

To: Edward Sassaman, MD
240 Turnpike Street
Canton, MA 02021

From: Children's Hospital
Emergency Department

Sent Via: FAX - 781-828-7541

Date: [redacted], 2009

Subj: G[redacted] T[redacted]
MR#: [redacted]
DOB: [redacted]
Tel#: (781)830-7856

Your patient, G[redacted] T[redacted], has been admitted to Children's Hospital on [redacted], 2009 with a diagnosis of CEREBRAL VASCULAR ACCIDENT.

G[redacted] is located on 9 North/West at (617)355-8096 under the attending care of Dr. David Coulter. You will be hearing from Dr. Coulter, who can also be reached at (617)355-6388.

If you need any further assistance, or if you are not the patient's primary or referring physician, please contact Children's Hospital at (617)355-6644 to ensure we have the correct provider information for this patient.

CHILDREN'S HOSPITAL EMERGENCY DEPARTMENT
300 Longwood Avenue, Boston, MA 02115
617-355-6611

To: Edward Sassaman, MD
240 Turnpike Street
Canton, MA 02021

Date: July 29, 2009

Last Name: T[redacted] First Name: G[redacted]
Patient DOB: [redacted] MR#: [redacted]
Date of Service: [redacted]/2009 Sex: M Tel#: (781)830-7856

CC: limp
HPI: 15 Year old male presents with limp. Per pt's caretakers, he was noted to have onset of limp on 7/11. He was favoring his right leg but was continuing to bear weight. He has a history of head banging at baseline and had a prolonged episode of banging on 7/13 for which he was evaluated at an OSH and found not to have any evidence of new injury or focal neurologic findings. He was then noted to have worsening of his limp and was seen at OSH on 7/18 where he had a normal CBC, normal ESR and CRP was not able to be performed. He had xrays of the hip that were normal and he was discharged home. He was then seen at CHB and felt to have isolated RLE limp without other abnormal findings. Since that visit, the limp has been worsening and the family has noted abnormal position of the RUE.

ROS:urination patterns dysfunctional with difficulty urinating and frequent urination

PMHx:Ex FT, autism with frequent head banging
Medications:none
Allergies: none
Immunizations:UTD
Soc Hx: lives at facility

VSS: 35.9 HR 68 RR 20 wt 65.9kg
General: awake, alert, no distress
HEENT: EOMI, PERRLA, moist mucous membranes
Neck: no lymphadenopathy
CV: RRR, S1/S2, no murmur
Resp: clear bilaterally
Abd: soft, NT/ND, positive bowel sounds, no organomegaly
GU: tanner 5 male, slight scrotal asymmetry, testicles with normal position, no pain on exam
Ext: moving all extremities symmetrically; full range of motion of

the arms, no joint effusions, slight decrease in ext rotation of the right hip-(last 10 degrees), no pain on palpation of the hips and lower extremities
neuro: CN 2-12 intact, gait asymmetric with internal right lower ext without favoring of either side of the foot; sensation and strength of bilateral upper and lower extremities intact; responsive to verbal stimuli as per baseline; while ambulating holding right upper ext in flexion at the elbow

ED course:
Pt evaluated by neurology and felt that findings were concerning for a stroke.
Had head CT that did not show infarct and was admitted to the neurology service for further evaluation.
CBC, chem and CK pending at the time of admission.

Dispo:Pt in stable condition at the time of admission wtih plan for further evlauation by neruology with likely MRI
Assessment: Abnormal gait, neurologic disturbance

ATTENDING NOTE:
I have obtained the history and examined the patient. I have reviewed the notes and agree with the history. Social and Family history noncontributory. ROS reviewed and negative. My examination of the patient revealed him to be active, alert, and in no distress. The HEENT exam was clear, the neck was supple, the lungs clear to auscultation, no abnormal cardiac sounds, the abdomen was nontender throughout. Gait is unsteady. left leg seems weak. left arm is held flexed at elbow and wrist, by history has difficulty urinating. Symptoms have come on over several days. Seen by neurology who believe this is stroke. Neurlogy fellow discussed with Dr. Coulter who accepts to service. Head Ct shows no acute hemorhage.

Assessment:

1. Limp. (Uncoded).
2. Eval for cerebral infarction

Electronically signed by Robert Wright, MD.

EXHIBIT 30

Eur Child Adolesc Psychiatry (2009)
18:458–463 DOI 10.1007/s00787-009-0754-8

CASE REPORT

ECT for self-injury in an autistic boy

Lee E. Wachtel
Stephanie A. Contrucci-Kuhn
Merrie Griffin
Ainsley Thompson
Dirk M. Dhossche
Irving M. Reti

Received: 12 November 2008
Accepted: 9 January 2009
Published online: 5 February 2009

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Department of Psychiatry
University of Mississippi Medical Center
2500 North State St.
Jackson, MS 39216, USA

I.M. Reti, MBBS
Department of Psychiatry
Johns Hopkins School of Medicine
600 N. Wolfe St., Meyer 3-181
Baltimore, MD 21205, USA

Abstract *Objective* Self-injurious behavior presents a significant challenge in autism, and first-line psychopharmacological and behavioral interventions have limited efficacy in some patients. These intractable cases may be responsive to electroconvulsive therapy. *Clinical picture* This article presents an eight-year-old boy with autism, mental retardation, prominent mood lability and a five-year history of extreme self-injurious behavior towards his head, averaging 109 self-injurious attempts hourly. The patient was at high risk for serious head trauma, and required usage of bilateral arm restraints and protective equipment (i.e., padding on shoulders, arms, and legs). All areas of daily functioning were profoundly impacted by dangerous self-injury. *Treatment* Fifteen bilateral ECT treatments resulted in excellent mood stabilization and reduction of self-injury to 19 attempts hourly, and maintenance ECT was pursued. The patient was able to return to developmentally-appropriate educational and social activities. *Conclusion* ECT should be considered in the treatment algorithm of refractory cases of severe self-injury in autism.

Key words self-injury – autism – ECT – mental retardation – catatonia

Introduction

Classically defined as *any act directed towards oneself that results in tissue damage* [38], self-injury occurs regularly in individuals with autism and other developmental disabilities, with prevalence rates ranging from 5 to 66% [10, 36]. Self-injury varies widely in frequency and intensity, and has the potential to cause crippling and life-threatening bodily injury and death, as well as impair interpersonal, social, educational and occupational functioning with increased risk for institutional placement [10, 27, 31].

Multiple biological [1, 11, 36] and psychological [2, 19] theories have been postulated to explain self-injury in autism and other developmental disabilities, and proposed treatments for self-injury are accordingly myriad.

Psychopharmacological interventions reported to have efficacy in some cases include antipsychotics, antidepressants, anxiolytics, anticonvulsants, opioid antagonists and antihypertensives [1, 11, 29]. Cur-

ECAP 754

rently, risperidone is the only drug with a US Federal Drug Administration indication for self-injury in autism, approved after a multi-site clinical trial in autistic children conducted by the Research Units on Pediatric Psychopharmacology [30]. When self-injury is considered as part of the catatonic syndrome, benzodiazepines and/or electroconvulsive therapy (ECT) may offer reduction of this harmful, repetitive motor activity [18, 19].

Although psychopharmacological agents are commonly tried for self-injury, medication interventions in autism are often limited by a high rate of adverse effects [2], and some suggest that psychotropic interventions for self-injury may produce effects simply through sedation and chemical restraint, leading to excessive medication prescription and polypharmacy [1, 29, 41]. Outcome measures reported for behavioral interventions for self-injury suggest a high degree of effectiveness [24], yet treatment failures may well be underreported in the literature [23], and clearly not all patients are responsive to behavioral interventions.

Thus, self-injury may remain resistant to psychotropic and behavioral interventions. The following case demonstrates that ECT may have a role in the resolution of intractable self-injury.

Case report

We report an eight-year-old male with autism and mental retardation who presented with a five-year history of self-injury towards his head. Self-injury included slapping and punching his head as well as banging his head on his knees and shoulders, with daily rates averaging 109.3 attempts hourly based on 24-h data collection. On daily mental status examination, D. presented as an adorable little boy without any evident dysmorphology who chronically demonstrated multiple areas of erythema, edema and callous formation on his forehead and cheeks. While wearing bilateral arm restraints as well as arm and leg sports padding, D. repeatedly would strike his straightened arm to his head, strike his knees to his head, and hit his head and ears onto his shoulders. Without arm restraints or protective equipment, D. would immediately commence striking his forehead, cheeks and nose with a closed fist and the resounding crack of bone hitting bone.

D.'s self-injury severely impacted all areas of daily functioning. D. had never been able to participate in a structured learning environment at school or home due to ongoing self-injury, and his learning potential was completely unknown. Play and social activities were similarly interrupted by self-injury, and D.'s family functioning was sharply impacted. D. was also unable to undertake any self-care alone, even requiring hand-over-hand shadowing during all meals to block head blows while self-feeding.

D. had undergone extensive applied behavioral assessments along with behavioral and medication trials for 3 years without any sustained reduction in self-injury. Psychotropic trials included sertraline, fluoxetine, clomipramine, valproic acid, lithium carbonate, carbamazepine, oxcarbazepine, gabapentin, aripiprazole, quetiapine, risperidone, olanzapine, haloperidol, fluphenazine, propranolol, lorazepam and clozapine. Both sertraline and fluoxetine led to prominent agitation and behavioral exacerbation, clomipramine and fluphenazine led to transient, small reductions in self-injury, and the remaining medications had no impact on behavioral rates. An adequate lorazepam challenge for potential catatonia was unable to be completed due to development of disinhibition and associated increased irritability and rates of self-injury at a dosage of 1 mg thrice daily. D. participated in outpatient and inpatient behavioral assessments and interventions including, but not limited to multiple functional analyses, antecedent analyses, preference assessments, reinforcement based interventions (i.e., functional communication training, differential reinforcement procedures, noncontingent reinforcement), response reduction procedures (i.e., brief physical holds, contingent application of helmet), and bilateral arm restraints and protective equipment (i.e., padding). Although several interventions initially resulted in behavioral reductions, the effects were not long-lasting.

D. also exhibited significant mood instability characterized by irritability, tantrumming, alternating laughing and crying episodes as well as intermittent insomnia and anorexia. Negative affect was correlated with increased rates of self-injury. Medical history was noncontributory, although family history was positive for paternal grandfather requiring ECT for severe depression. D. did not evince any classic signs of catatonia, including posturing, echophenomena, rigidity, waxy flexibility, mutism (D. had never been verbal) or autonomic instability. However, he clearly demonstrated ongoing, stereotyped repetitive movements in the form of self-injury, as well as the above-noted periods of agitation.

Continuous self-injury of the head had required 24-h placement of D. in bilateral arm restraints with rigid metal stays, a cervical immobilizer as well as upper and lower extremity padding with protective sports equipment. Attempts at self-injury continued despite this highly restrictive situation, and a course of ECT was pursued.

European Child & Adolescent Psychiatry (2009) Vol. 18, No. 7

Methods

Consent for ECT was obtained from D.'s parents after review by two child psychiatrists not involved with his care. A pediatric neurologist was also consulted as part of routine work-up and to review his seizure response. Modified ECT was supervised by Dr IR and administered with a MECTA Spectrum 5000Q unit. Anesthesia was induced by methohexital 50 mg iv, and succinylcholine 10 mg iv was administered for muscle relaxation. We opted for bitemporal electrode placement in light of prior case reports of both children and developmentally delayed adults with self-injury being successfully treated with bitemporal placement. Seizure activity was monitored clinically and by bifrontal EEG. Recorded seizure length was ascertained by EEG. Seizure threshold was estimated at 56 millicoloumbs (mC) and 15 treatments were administered over 5 weeks on a thrice weekly schedule during the acute course before tapering was commenced. Mean charge administered over the acute course was 168mC and average seizure length was 145 s. On three occasions seizures were terminated by propofol 15 mg iv when they exceeded 180 s.

Results

A profound reduction in rates of self-injury was observed in D. after the first ECT treatment. Upon waking, D.'s arm restraints were not immediately replaced and for a full ninety minutes D. was observed to not engage in a single episode of self-injury. He sat calmly in his bed, smiled and looked around his room, then rose to run about the unit with outward laughing. This result was astounding, in that prior to ECT, D. had consistently engaged in high-frequency and high-intensity hand-to-head SIB within seconds of arm restraint removal, leading to rapid facial edema and erythema, as well as frequent nose bleeds.

A consistent significant reduction in SIB was observed over the next 5 weeks while D. continued to receive bilateral ECT thrice weekly. Specifically, prior to the initiation of ECT, rates of self-injury were 100.6 h while wearing restraints and 109.3 h without restraint. During the reported phase of the first 5 weeks of ECT, rates of self-injury were reduced to 6.5 h with restraints and 19.4 h without restraints. Restraints after ECT consisted *only* of empty canvas sleeves (i.e. without the prior rigid metal stays in the sleeves, cervical immobilizer and full limb padding). See Fig. 1.

In addition to the reduction in SIB, D. was also able for the first time in his life to reliably engage in both

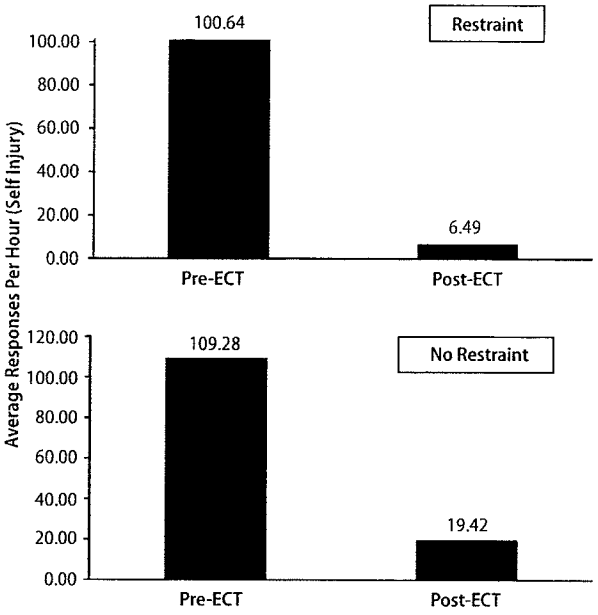

Fig. 1 Rates of self-injury before and after ECT

play and educational activities. D. was able to consistently work on daily structured academic tasks, thus affording his first opportunity to work on developmentally-appropriate educational goals with much potential for improved future functioning. He was also able to engage in meaningful family activities to the profound astonishment of his parents.

Due to the unknown effects of ECT on the brain of a nine-year-old, a repeat brain MRI post-ECT was obtained. It showed no changes compared with the pre-ECT MRI.

Discussion

As far as we are aware, this is the first published case report of intractable self-injury in a disabled prepubertal child being treated successfully with ECT. Only three English-language reports exist of ECT being used expressly for self-injury, one in an adolescent and two in an adult. A 14-year-old male with mental retardation, persistent headbanging and self-scratching had reduction of both topographies with bilateral ECT [18], a 25-year-old adult male with severe mental retardation and a several year history of head self-injury also showed remission with bilateral ECT [6], and a 32-year-old adult male with normal cognition, bipolar psychotic depression and multiple topographies of self-mutilation demonstrated excellent response to ECT [4]. There is also additional literature of successful ECT usage in children and

adolescents with pediatric psychotic or catatonic affective illnesses that were complicated by additional symptoms of self-injury. Carr et al. [13.] present a 12-year-old girl with bipolar affective disorder and concomitant body slamming self-injury, Black et al. [9] report an 11-year-old boy with depression, headbanging and self-biting, Cizadlo and Wheaton [15] discuss an eight-year-old girl with depression, catatonia and hand-to-head self-injury, Wachtel et al. [42] present an 18-year-old girl with autism, catatonia and severe hand-head self-injury resulting in nearly complete blindness from retinal detachment and Chung & Varghese [14] report an 11-year-old girl with psychosis, catatonia, headbanging and self-scratching. Over half century ago, Stauder also reported young adults with lethal catatonia who further demonstrated self-injury [37], and Leonhard vividly described self-injury in his writings on childhood catatonia [28]. Although the above reports present self-injury as an additional symptom along with catatonia, a more comprehensive conceptualization might consider self-injury as an integral part of the catatonic constellation.

Indeed, the question of catatonia as a possible etiology for D.'s extreme rates of self-injury is intriguing. Current thought supports the existence of catatonia as its own entity, with a myriad of psychiatric, neurological, medical and drug-related causative factors [3, 19]. Comprehensive catatonia rating scales such as the Bush-Francis Catatonia Rating Scale include symptoms such as excitement and motor unrest, stereotypy, mannerisms, impulsivity and sudden engagement in inappropriate behavior, as well as combativeness with potential for harm [12]. We believe that self-injury such as that demonstrated by D. would clearly meet such criteria.

Furthermore, catatonia is known to occur most commonly in bipolar affective illness [19], and D.'s ongoing mood lability, irritability, sleep disturbance and family history supported a potential bipolar diagnosis. Additionally, catatonia has been discovered to occur in autistic individuals like D. at increased rates of 12–17%, with ECT included in the current treatment guidelines if lorazepam fails [8, 20, 46].

Self-injury may also be explained in some cases by monoamine dysfunction, which can conceivably be reversed by ECT. For example, ECT has been shown to increase GABAergic transmission [34] which may ameliorate lack of GABA inhibition associated with SIB [36]. Similarly, decreased dopamine and serotonin function associated with SIB [36] may be rectified by ECT [47]. Additionally, theories of ECT's overall effectiveness discuss the hypothalamic release of neurohumors previously lacking in the patient's brain, as well as an overall normalization of the hypothalamic-pituitary-adrenal (HPA) axis [18]. This may be particularly salient in D.'s case, and we question whether ECT may also cause the release of a neurohumor or neurohumoral cascade with beneficial effects on self-injury. Finally, there is evidence in both primates and humans with developmental disabilities that HPA-axis dysfunction, specifically the uncoupling of proopiomelanocortin (POMC)-derived stress hormones, is a correlate of self-injury [26, 35, 40]. Possibly, peripheral uncoupling may reflect central dysregulation of the HPA axis which is sensitive to the therapeutic effects of ECT [48].

Although ECT in adolescents has proven to be safe and effective [43, 44], its use in prepubertal children has been controversial. D.'s case was no exception, with many concerns raised regarding the usage of ECT in a developmentally disabled eight-year-old, the unknown later effects on his developing brain and possible legal issues. Much of this may have been fueled by anti-ECT prejudice which continues to plague psychiatry, often preventing prompt access to life-saving treatment. Ironically, the efficacious and safe usage of ECT in children with affective and psychotic illness has been documented since the 1940s [7, 22]. Modern ECT case reports in children aged 6–12 offer further support for its resolution of pediatric psychotic or catatonic affective illness [13, 15, 17, 33, 45].

The literature also supports the safe and successful usage of ECT in the mentally retarded population. Multiple case reports review the usage of ECT for affective, psychotic and catatonic illness in mentally retarded adults [5, 32, 39]. There also exists a growing body of literature on ECT usage in mentally retarded adolescents, particularly autistic adolescents with catatonic deterioration [16, 20, 21, 25, 42, 49]. We believe that the scientific support of ECT in normally-developing pediatric, adolescent and adult patients, as well as adolescent and adult mentally retarded individuals should be extended to the pre-pubertal mentally retarded population, particularly in cases of dire need such as D.

We believe as well that the potential benefits of ECT in this case significantly outweighed the standard ECT and anesthesia risks as well as the "element of the unknown" in terms of longterm effects of ECT on D.'s developing brain. Having already failed years of behavioral and pharmacological therapy, D. was otherwise destined to (a) remain immobilized in full-body restraint, or (b) continue to engage in extreme rates of self-injury towards his head, with obvious long-term risk for intracranial damage. ECT proved to be truly life-saving in this case, affording a severely disabled child the opportunity to resume his developmental trajectory and reintegrate into life outside a locked inpatient unit.

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Conclusions

Self-injury is a dangerous and sharply impairing condition that afflicts many individuals with developmental disabilities. Psychiatric, behavioral, neurochemical and neuroendocrine conditions have all been proposed as potentially explanatory. Additionally, self-injury may also represent a symptom of catatonia as a repetitive and purposeless motoric activity that may be associated with other catatonic, affective or psychotic symptomology. Recognition of this option should invoke a lorazepam trial at adequate dosages, followed by consideration of ECT if the former is ineffective. Judicious usage of ECT in the developmentally-disabled population with severe self-injury may afford a significant opportunity for recovery. Further research into the concomitance of self-injury and catatonia is warranted.

References

1. Aman MG, Collier-Crespin A, Lindsay RL (2000) Pharmacotherapy of disorders in mental retardation. Eur Child Adolesc Psychiatry 9:I98–I107
2. American Association on Mental Retardation (2000) Treatment of psychiatric and behavioral problems in mental retardation. Am J Ment Retard 105:165–188
3. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, 4th edn. American Psychiatric Association, Washington, DC
4. Arora M, Praharaj SK, Prakash R (2008) Electroconvulsive therapy for multiple major self-mutilations in bipolar psychotic depression. Turk J Psychiatry 19(2):1–4
5. Aziz M, Maixner D, DeQardo J, Aldridge A, Tandon R (2001) ECT and mental retardation: a review and case report. J ECT 17:149–152
6. Bates W, Smeltzer D (1982) Electroconvulsive treatment of psychotic self-injurious behavior in a patient with severe mental retardation. Am J Psychiatry 139:1355–1356
7. Bender L (1947) One hundred cases of childhood schizophrenia treated with electric shock. Trans Am Neurol Soc 72:165–169
8. Billstedt E, Gilberg C, Gilberg C (2005) Autism after adolescence: population-based 13- to 22-year follow-up study of 120 individuals with autism diagnosed in childhood. J Autism Dev Disord 35:351–360
9. Black D, Wilcox J, Stewart M (1985) The use of ECT in children: case-report. J Clin Psychiatry 46:98–99
10. Borthwick-Duffy SA (1994) Epidemiology and prevalence of psychopathology in people with mental retardation. J Consult Clin Psychol 62(1):17–27
11. Buitelaar JK, Willemsen-Swinkels SHN (2000) Medication treatment in subjects with autism spectrum disorders. Eur Child Adolesc Psychiatry 9:I85–I97
12. Bush G, Fink M, Petrides G, Dowling F, Francis A (1996) Catatonia. I: rating scale and standardized examination. Acta Psychiatr Scand 93:129–136
13. Carr V, Dorrington C, Schrader G, Wale J (1983) The use of ECT for mania in childhood bipolar disorder. Br J Psychiatry 143:411–415
14. Chung A, Varghese J (2008) Treatment of catatonia with electroconvulsive therapy in an 11-year-old girl. Aust NZ J Psychiatry 42:251–253
15. Cizadlo B, Wheaton A (1995) Case study: ECT treatment of a young girl with catatonia. J Am Acad Child Adolesc Psychiatry 34:332–335
16. Dhossche D, Shah A, Wing L (2006) Blueprints for the assessment, treatment, and future study of catatonia in autism spectrum disorders. Int Rev Neurobiol 72:267–284
17. Esmaili T, Malek A (2007) Electroconvulsive therapy (ECT) in a six-year-old girl suffering from major depressive disorder with catatonic features. Eur Child Adolesc Psychiatry 16:58–60
18. Fink M (1999) Electroshock: healing mental illness. Oxford University Press, London
19. Fink M, Taylor M (2003) Catatonia: a clinician's guide to diagnosis and treatment. University Press, Cambridge
20. Fink M, Taylor M, Ghaziuddin N (2006) Catatonia in autistic spectrum disorders: a medical treatment algorithm. Int Rev Neurobiol 72:233–244
21. Ghaziuddin M, Quinlan P, Ghaziuddin N (2005) Catatonia in autism: a distinct subtype? J Intell Disabil Res 49:102–105
22. Heuyer G, Bour, Leroy R (1943) L'electrochoc chez les enfants. Ann Med Psychol (Paris) 2:402–407
23. Johnson WL, Baumeister AA (1978) Self-injurious behavior: a review and analysis of methodological details of published studies. Behav Modif 2:465–487
24. Kahng SWIB, Lewin AB (2002) Behavioral treatment of self-injury, 1964–2000. Am J Ment Retard 107(3):212–221
25. Kakooza-Mwesige A, Wachtel L, Dhossche D (2008) Catatonia in autism: implications across the life span. Eur Child Adolesc Psychiatry 17(6):327–335
26. Kemp ASFP, Lenjavi MR, Lyon M, Chicz-DeMet A, Touchette PE, Sandman CA (2007) Temporal patterns of self-injurious behavior correlate with stress hormone levels in the developmentally disabled. Psychiatry Res 157:181–189
27. King BH, Cromwell HC, Lee HT, Behrstock SP, Schmanke T, Maidment NT (1998) Dopaminergic and glutamatergic interactions in the expression of self-injurious behavior. Dev Neurosci 20:180–187
28. Leonhard K (1979) The classification of endogenous psychoses. In: Robins E (ed). Irvington, New York
29. Matson JLBJ, Mayville EA, Pinkston J, Bielecki J, Kuhn DE, Smalls Y, Logan JR (2000) Psychopharmacology and mental retardation: a 10 year review. Res Dev Disabil 21:263–296
30. McDougle CJSL, Aman MG, McCracken JT, Tierney E, Davies M, Arnold LE, Posey DJ, Martin A, Ghuman JK, Shah B, Chuang SZ, Swiezy NB, Gonzalez NM, Hollway J, Koenig K, McGough JJ, Ritz L, Vitiello B (2005) Risperidone for the core symptoms of autism: results from the study by the autism network of the research units on pediatric psychopharmacology. Am J Psychiatry 162(6):1142–1148
31. Paclawskyj TR, Kurtz PF, O'Connor JT (2004) Functional assessment of problem behaviors in adults with mental retardation. Behav Modif 28(5):649–667
32. Reinblatt S, Rifkin A, Freeman J (2004) The efficacy of ECT in adults with mental retardation experiencing psychiatric disorders. J ECT 20:208–212
33. Russell P, Tharyan P, Arun Kumar K, Cherian A (2002) Electroconvulsive therapy in a pre-pubertal child with severe depression. J Postgrad Med 48:290–291

34. Sanacora G, Mason G, Rothman D, Hyder F, Ciarcia J, Ostroff R, Berman R, Krystal J (2003) Increased cortical GABA concentrations in depressed patients receiving ECT. Am J Psychiatry 160:577–579
35. Sandman C, Touchette P, Lenjavi M, Marion S, Chicz-DeMet A (2003) B-endorphin and ACTH are dissociated after self-injury in adults with developmental disabilities. Am J Ment Retard 108:414–424
36. Schroeder S, Oster-Granite M, Berkson G, Bodfish J, Breese G, Cataldo M, Cook E, Crnic L, DeLeon I, Fisher W, Harris J, Horner R, Iwata B, Jinnah H, King B, Lauder J, Lewis M, Newell K, Nyhan W, Rojahn J, Sackett G, Sandman C, Symons F, Tessel R, Thompson T, Wong D (2001) Self-injurious behavior: gene-brain-behavior relationships. Ment Retard Dev Disabil Res Rev 17:3–12
37. Stauder K (1934) Die todliche Katatonie. Arch Psychiatr Nervenkrank 102:614–634
38. Tate BG, Baroff GS (1966) Aversive control of self-injurious behavior in a psychotic boy. Behav Res Ther 4(4):281–287
39. Thuppal M, Fink M (1999) Electroconvulsive therapy and mental retardation. J ECT 15:140–149
40. Tiefenbacher S, Novak M, Marinus L, Chase W, Miller J, Meyer J (2004) Altered hypothalamic-pituitary-adrenocortical function in rhesus monkeys (Macaca mulatta) with self-injurious behavior. Psychoneuroendocrinology 29:501–515
41. Wachtel LE, Hagopian LP (2006) Psychopharmacology and applied behavioral analysis: tandem treatment of severe problem behaviors in intellectual disability and a case series. Isr J Psychiatry Relat Sci 43(4):265–274
42. Wachtel L, Kahng S, Dhossche D, Cascella N, Reti I (2008) Electroconvulsive therapy for catatonia in an autistic girl. Am J Psychiatry 165:329–333
43. Walter G, Rey J (1997) An epidemiological study of the use of ECT in adolescents. J Am Acad Child Adolesc Psychiatry 36:809–815
44. Walter G, Koster K, Rey J (1999) Electroconvulsive therapy in adolescents: experience, knowledge, and attitudes of recipients. J Am Acad Child Adolesc Psychiatry 38:594–599
45. Willoughby C, Hradek E, Richards N (1997) Use of electroconvulsive therapy with children: an overview and case report. J Child Adolesc Psychiatr Nurs 10:11–17
46. Wing L, Shah A (2000) Catatonia in autistic spectrum disorders. Br J Psychiatry 176:357–362
47. Yoshida K, Higuchi H, Kamata M, Yoshimoto M, Shimizu T, Hishikawa Y (1998) Single and repeated electroconvulsive shocks activate dopaminergic and 5-hydroxytryptaminergic neurotransmission in the frontal cortex of rats. Prog Neuropsychopharmacol Biol Psychiatry 22:435–444
48. Yuuki N, Ida I, Oshima A, Kumano H, Takahashi K, Fukuda M, Oriuchi N, Endo K, Matsuda H, Mikuni M (2005) HPA axis normalization, estimated by DEX/CRH test, but less alteration on cerebral glucose metabolism in depressed patients receiving ECT after medication treatment failures. Acta Psychiatr Scand 112:257–265
49. Zaw F, Bates G, Murali V, Bentham P (1999) Catatonia, autism, and ECT. Dev Med Child Neurol 41:843–845

EXHIBIT 31

Mental Health

A Report of the Surgeon General
Executive Summary

DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. Public Health Service

The Center for Mental Health Services
Substance Abuse and Mental Health Services Administration

National Institute of Mental Health
National Institutes of Health

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Outpatient Treatment. In outpatient clinical trials, about 50 to 70 percent of depressed patients who complete treatment respond to either antidepressants or psychotherapies (Depression Guideline Panel, 1993). An acute treatment response includes the effects of placebo expectancy, spontaneous remission, and active treatment. The magnitude of the active treatment effect may be estimated from randomized clinical trials by subtracting the placebo response rate from that of active medication. Overall, the active treatment effect for major depression typically ranges from 20 to 40 percent, after accounting for a placebo response rate of about 30 percent (Depression Guideline Panel, 1993). Although psychotherapy trials do not employ placebos in the form of an inert pill, they do rely on comparisons of active treatment with psychological placebos (e.g., a form of therapy inappropriate for a given disorder), a comparison form of treatment, or wait list (i.e., no therapy). The figures cited above must be understood as rough averages. The efficacy of specific pharmacotherapies and psychotherapies is covered later in this section.

Acute phase therapy is often compromised by patients leaving treatment. Attrition rates from clinical trials often are as high as 30 to 40 percent, and rates of nonadherence[10] are even higher (Depression Guideline Panel, 1993). Medication side effects are a factor, as are other factors such as inadequate psychoeducation (resulting in unrealistic expectations about treatment), ambivalence about seeing a therapist or taking medication, and practical roadblocks (e.g., the cost or accessibility of services).

Another problem is clinician failure to monitor symptomatic response and to change treatments in a timely manner. Antidepressants should be changed if there is no clear effect within 4 to 6 weeks (Nierenberg et al., 1995; Quitkin et al., 1996). Similar data are not available for psychotherapies, but revisions to the treatment plan should be considered, including the addition of antidepressant medication, if there is no symptomatic improvement within 3 or 4 months (Depression Guideline Panel, 1993).

Acute Inpatient Treatment. Hospitalization for acute treatment of depression is necessary for about 5 to 10 percent of major depressive episodes and for up to 50 percent of manic episodes. The principal reasons for hospitalization are overwhelming severity of symptoms and functional incapacity and suicidal or other life-threatening behavior. Hospital median lengths of stay now are about 5 to 7 days for depression and 9 to 14 days for mania. Such abbreviated stays have reduced costs but necessitate greater transitional or aftercare services. Few severely depressed or manic people are in remission after only 1 to 2 weeks of treatment.

Electroconvulsive Therapy. As described above, first-line treatment for most people with depression today consists of antidepressant medication, psychotherapy, or the combination (Potter et al., 1991; Depression Guideline Panel, 1993). In situations where these options are not effective or too slow (for example, in a person with delusional depression and intense, unremitting suicidality) electroconvulsive therapy (ECT) may be considered. ECT, sometimes referred to as *electroshock* or *shock treatment,* was developed in the 1930s based on the mistaken belief that epilepsy (seizure disorder) and schizophrenia could not exist at the same time in an individual. Accumulated clinical experience—later confirmed in controlled clinical trials, which included the use of simulated or "sham" ECT as a control (Janicak et al., 1985)—determined ECT to be highly effective against severe depression, some acute psychotic states, and mania (Small et al., 1988). No controlled study has shown any other treatment to have superior efficacy to ECT in the treatment of depression (Janicak et al., 1985; Rudorfer et al., 1997). ECT has not been demonstrated to be effective in dysthymia, substance abuse, or anxiety or personality disorders. The foregoing conclusions, and many of those discussed below, are the products of review of extensive research conducted over several decades (Depression Guideline Panel, 1993; Rudorfer et al., 1997) as well as by an independent panel of

[10] Nonadherence is defined as lack of adherence to prescribed activities such as keeping appointments, taking medication, and completing assignments.

scientists, practitioners, and consumers (NIH & NIMH Consensus Conference, 1985).

ECT consists of a series of brief generalized seizures induced by passing an electric current through the brain by means of two electrodes placed on the scalp. A typical course of ECT entails 6 to 12 treatments, administered at a rate of three times per week, on either an inpatient or outpatient basis. The exact mechanisms by which ECT exerts its therapeutic effect are not yet known. The production of an adequate, generalized seizure using the proper amount of electrical stimulation at each treatment session is required for therapeutic efficacy (Sackheim et al., 1993).

With the development of effective medications for the treatment of major mental disorders a half-century ago, the need for ECT lessened but did not disappear. Prior to that time, ECT often had been administered for a variety of conditions for which it is not effective, and administered without anesthesia or neuromuscular blockade. The result was grand mal seizures that could produce injuries and even fractures. Despite the availability of a range of effective antidepressant medications and psychotherapies, as discussed above, ECT continues to be used (Rosenbach et al., 1997), occupying a narrower but important niche. It is generally reserved for the special circumstances where the usual first-line treatments are ineffective or cannot be taken, or where ECT is known to be particularly beneficial, such as depression or mania accompanied by psychosis or catatonia (NIH & NIMH Consensus Conference, 1985; Depression Guideline Panel, 1993; Potter & Rudorfer, 1993). Examples of specific indications include depression unresponsive to multiple medication trials, or accompanied by a physical illness or pregnancy, which renders the use of a usually preferred antidepressant dangerous to the patient or to a developing fetus. Under such circumstances, carefully weighing risks and benefits, ECT may be the safest treatment option for severe depression. It should be administered under controlled conditions, with appropriate personnel (Rudorfer et al., 1997).

Although the average 60 to 70 percent response rate seen with ECT is comparable to that obtained with pharmacotherapy, there is evidence that the antidepressant effect of ECT occurs faster than that seen with medication, encouraging the use of ECT where depression is accompanied by potentially uncontrollable suicidal ideas and actions (Rudorfer et al., 1997). However, ECT does not exert a long-term protection against suicide. Indeed, it is now recognized that a single course of ECT should be regarded as a short-term treatment for an acute episode of illness. To sustain the response to ECT, continuation treatment, often in the form of antidepressant and/or mood stabilizer medication, must be instituted (Sackeim, 1994). Individuals who repeatedly relapse following ECT despite continuation medication may be candidates for maintenance ECT, delivered on an outpatient basis at a rate of one treatment weekly to as infrequently as monthly (Sackeim, 1994; Rudorfer et al., 1997).

The major risks of ECT are those of brief general anesthesia, which was introduced along with muscle relaxation and oxygenation to protect against injury and to reduce patient anxiety. There are virtually no absolute health contraindications precluding its use where warranted (Potter & Rudorfer, 1993; Rudorfer et al., 1997).

The most common adverse effects of this treatment are confusion and memory loss for events surrounding the period of ECT treatment. The confusion and disorientation seen upon awakening after ECT typically clear within an hour. More persistent memory problems are variable. Most typical with standard, bilateral electrode placement (one electrode on each side of the head) has been a pattern of loss of memories for the time of the ECT series and extending back an average of 6 months, combined with impairment with learning new information, which continues for perhaps 2 months following ECT (NIH & NIMH Consensus Conference, 1985). Well-designed neuropsychological studies have consistently shown that by several months after completion of ECT, the ability to learn and remember are normal (Calev, 1994). Although most patients return to full functioning following successful ECT, the degree of post-treatment memory impairment and resulting impact on functioning are highly variable

across individuals (NIH & NIMH Consensus Conference, 1985; CMHS, 1998). While clearly the exception rather than the rule, no reliable data on the incidence of severe post-ECT memory impairment are available. Fears that ECT causes gross structural brain pathology have not been supported by decades of methodologically sound research in both humans and animals (NIH & NIMH Consensus Conference, 1985; Devanand et al., 1994; Weiner & Krystal, 1994; Greenberg, 1997; CMHS, 1998). The decision to use ECT must be evaluated for each individual, weighing the potential benefits and known risks of all available and appropriate treatments in the context of informed consent (NIH & NIMH Consensus Conference, 1985).

Advances in treatment technique over the past generation have enabled a reduction of adverse cognitive effects of ECT (NIH & NIMH Consensus Conference, 1985; Rudorfer et al., 1997). Nearly all ECT devices deliver a lower current, *brief-pulse* electrical stimulation, rather than the original sine wave output; with a brief pulse electrical wave, a therapeutic seizure may be induced with as little as one-third the electrical power as with the older method, thereby reducing the potential for confusion and memory disturbance (Andrade et al., 1998). Placement of both stimulus electrodes on one side of the head ("unilateral" ECT), over the nondominant (generally right) cerebral hemisphere, results in delivery of the initial electrical stimulation away from the primary learning and memory centers. According to several controlled trials, unilateral ECT is associated with virtually no detectable, persistent memory loss (Horne et al., 1985; NIH Consensus Conference, 1985; Rudorfer et al., 1997). However, most clinicians find unilateral ECT less potent and more slowly acting an intervention than conventional bilateral ECT, particularly in the most severe cases of depression or in mania. One approach that is sometimes used is to begin a trial of ECT with unilateral electrode placement and switch to bilateral treatment after about six treatments if there has been no response. Research has demonstrated that the relationship of electrical dose to clinical response differs depending on electrode placement; for bilateral ECT, as long as an adequate seizure is obtained, any additional dosage will merely add to the cognitive toxicity, whereas for unilateral electrode placement, a therapeutic effect will not be achieved unless the electrical stimulus is more than minimally above the seizure threshold (Sackeim et al., 1993). Even a moderately high electrical dosage in unilateral ECT still has fewer cognitive adverse effects than bilateral ECT. On the other hand, high-dose bilateral ECT may be unnecessarily risky and may be a preventable cause of severe memory impairment. Some types of medication, such as lithium, also add to confusion and cognitive impairment when given during a course of ECT and are best avoided. Medications that raise the seizure threshold and make it harder to obtain a therapeutic effect from ECT, including anticonvulsants and some minor tranquilizers, may also need to be tapered or discontinued.

Informed consent is an integral part of the ECT process (NIH & NIMH Consensus Conference, 1985). The potential benefits and risks of this treatment, and of available alternative interventions, should be carefully reviewed and discussed with patients and, where appropriate, family or friends. Prospective candidates for ECT should be informed, for example, that its benefits are short-lived without active continuation treatment, and that there may be some risk of permanent severe memory loss after ECT. In most cases of depression, the benefit-to-risk ratio will favor the use of medication and/or psychotherapy as the preferred course of action (Depression Guideline Panel, 1993). Where medication has not succeeded, or is fraught with unusual risk, or where the potential benefits of ECT are great, such as in delusional depression, the balance of potential benefits to risks may tilt in favor of ECT. Active discussion with the treatment team, supplemented by the growing amount of printed and videotaped information packages for consumers, is necessary in the decisionmaking process, both prior to and throughout a course of ECT. Consent may be revoked at any time during a series of ECT sessions.

Although many people have fears related to stories of forced ECT in the past, the use of this modality on an involuntary basis today is uncommon. Involuntary

ECT may not be initiated by a physician or family member without a judicial proceeding. In every state, the administration of ECT on an involuntary basis requires such a judicial proceeding at which patients may be represented by legal counsel. As a rule, such petitions are granted only where the prompt institution of ECT is regarded as potentially lifesaving, as in the case of a person who is in grave danger because of lack of food or fluid intake caused by catatonia. Recent epidemiological surveys show that the modern use of ECT is generally limited to evidence-based indications (Hermann et al., 1999). Indeed, concern has been raised that in some settings, particularly in the public sector and outside major metropolitan areas, ECT may be underutilized due to the wide variability in the availability of this treatment across the country (Hermann et al., 1995). Consequently, minority patients tend to be underrepresented among those receiving ECT (Rudorfer et al., 1997).

On balance, the evidence supports the conclusion that modern ECT is among those treatments effective for the treatment of select severe mental disorders, when used in accord with current standards of care, including appropriate informed consent.

Continuation Phase Therapy

Successful acute phase antidepressant pharmacotherapy or ECT should almost always be followed by at least 6 months of continued treatment (Prien & Kupfer, 1986; Depression Guideline Panel, 1993; Rudorfer et al., 1997). During this phase, known as the continuation phase, most patients are seen biweekly or monthly. The primary goal of continuation pharmacotherapy is to prevent relapse (i.e., an exacerbation of symptoms sufficient to meet syndromal criteria). Continuation pharmacotherapy reduces the risk of relapse from 40-60 percent to 10-20 percent (Prien & Kupfer, 1986; Thase, 1993). Relapse despite continuation pharmacotherapy might suggest either nonadherence (Myers & Branthwaithe, 1992) or loss of a placebo response (Quitkin et al., 1993a).

A second goal of continuation pharmacotherapy is consolidation of a response into a complete remission and subsequent recovery (i.e., 6 months of sustained remission). A remission is defined as a complete resolution of affective symptoms to a level similar to healthy people (Frank et al., 1991a). As residual symptoms are associated with increased relapse risk (Keller et al., 1992; Thase et al., 1992), recovery should be achieved before withdrawing antidepressant pharmacotherapy.

Many psychotherapists similarly taper a successful course of treatment by scheduling several sessions (every other week or monthly) prior to termination. There is some evidence, albeit weak, that relapse is less common following successful treatment with one type of psychotherapy—cognitive-behavioral therapy—than with antidepressants (Kovacs et al., 1981; Blackburn et al., 1986; Simons et al., 1986; Evans et al., 1992). If confirmed, this advantage may offset the greater short-term costs of psychotherapy.

Maintenance Phase Therapies

Maintenance pharmacotherapy is intended to prevent future recurrences of mood disorders (Kupfer, 1991; Thase, 1993; Prien & Kocsis, 1995). A recurrence is viewed as a new episode of illness, in contrast to relapse, which represents reactivation of the index episode (Frank et al., 1991a). Maintenance pharmacotherapy is typically recommended for individuals with a history of three or more depressive episodes, chronic depression, or bipolar disorder (Kupfer, 1991; Thase, 1993; Prien & Kocsis, 1995). Maintenance pharmacotherapy, which may extend for years, typically requires monthly or quarterly visits.

Longer term, preventive psychotherapy to prevent recurrences has not been studied extensively. However, in one study of patients with highly recurrent depression, monthly sessions of interpersonal psychotherapy were significantly more effective than placebo but less effective than pharmacotherapy (Frank et al., 1991a).

Specific Treatments for Episodes of Depression and Mania

This section describes specific types of pharmacotherapies and psychosocial therapies for *episodes* of depression and mania. Treatment generally targets

symptom patterns rather than specific disorders. Differences in the treatment strategy for unipolar and bipolar depression are described where relevant.

Treatment of Major Depressive Episodes

Pharmacotherapies

Antidepressant medications are effective across the full range of severity of major depressive episodes in major depressive disorder and bipolar disorder (American Psychiatric Association, 1993; Depression Guideline Panel, 1993; Frank et al., 1993). The degree of effectiveness, however, varies according to the intensity of the depressive episode. With mild depressive episodes, the overall response rate is about 70 percent, including a placebo rate of about 60 percent (Thase & Howland, 1995). With severe depressive episodes, the overall response rate is much lower, as is the placebo rate. For example, with psychotic depression, the overall response rate to any one drug is only about 20 to 40 percent (Spiker, 1985), including a placebo response rate of less than 10 percent (Spiker & Kupfer, 1988; Schatzberg & Rothschild, 1992). Psychotic depression is treated with either an antidepressant/antipsychotic combination *or* ECT (Spiker, 1985; Schatzberg & Rothschild, 1992).

There are four major classes of antidepressant medications. The tricyclic and heterocyclic antidepressants (TCAs and HCAs) are named for their chemical structure. The MAOIs and SSRIs are classified by their initial neurochemical effects. In general, MAOIs and SSRIs increase the level of a target neurotransmitter by two distinct mechanisms. But, as discussed below, these classes of medications have many other effects. They also have some differential effects depending on the race or ethnicity of the patient.

The mode of action of antidepressants is complex and only partly understood. Put simply, most antidepressants are designed to heighten the level of a target neurotransmitter at the neuronal synapse. This can be accomplished by one or more of the following therapeutic actions: boosting the neurotransmitter's synthesis, blocking its degradation, preventing its reuptake from the synapse into the presynaptic neuron, or mimicking its binding to postsynaptic receptors. To make matters more complicated, many antidepressant drugs affect more than one neurotransmitter. Explaining how any one drug alleviates depression probably entails multiple therapeutic actions, direct and indirect, on more than one neurotransmitter system (Feighner, 1999).

Selection of a particular antidepressant for a particular patient depends upon the patient's past treatment history, the likelihood of side effects, safety in overdose, and expense (Depression Guideline Panel, 1993). A vast majority of U.S. psychiatrists favor the SSRIs as "first-line" medications (Olfson & Klerman, 1993). These agents are viewed more favorably than the TCAs because of their ease of use, more manageable side effects, and safety in overdose (Kapur et al., 1992; Preskorn & Burke, 1992). Perhaps the major drawback of the SSRIs is their expense: they are only available as name brands (until 2002 when they begin to come off patent). At minimum, SSRI therapy costs about $80 per month (Burke et al., 1994), and patients taking higher doses face proportionally greater costs.

Four SSRIs have been approved by the FDA for treatment of depression: fluoxetine, sertraline, paroxetine, and citalopram. A fifth SSRI, fluvoxamine, is approved for treatment of obsessive-compulsive disorder, yet is used off-label for depression.[11] There are few compelling reasons to pick one SSRI over another for treatment of uncomplicated major depression, because they are more similar than different (Aguglia et al., 1993; Schone & Ludwig, 1993; Tignol, 1993; Preskorn, 1995). There are, however, several distinguishing pharmacokinetic differences between SSRIs, including elimination half-life (the time it takes for the plasma level of the drug to decrease 50 percent from steady-state), propensity for drug-drug interactions (e.g., via inhibition of hepatic enzymes), and antidepressant activity of metabolite(s) (DeVane, 1992). In general, SSRIs are more likely to be

[11] Technically, FDA approves drugs for a selected indication (a disorder in a certain population). However, once the drug is marketed, doctors are at liberty to prescribe it for unapproved (off-label) indications.

EXHIBIT 32

...Elroy SL, Keck PE, Stanton SP, Tugrul KC, Bennett JA: A randomized comparison of divalproex oral loading vs. haloperidol in the initial treatment of acute psychotic mania. *J Clin Psychiatry*. 1996;57(4):142.

...Muller-Oerlinghausen B, Retzow A, Henn F, Giedke H, Walden J: Valproate as an adjunct to neuroleptic medication for the treatment of acute episodes of mania: A prospective, randomized, double-blind, placebo-controlled, multicenter study. *J Clin Psychopharmacol*. 2000;20:195.

...Donovan C, Kusumaker V, Graves GR, Bird DC: Menstrual abnormalities and polycystic ovary syndrome in women taking valproate for bipolar mood disorder. *J Clin Psychiatry*. 2002;63:322.

...ay F, Rush JA, Davis JM, Calabrese JR, Kimmel SE: Plasma GABA predicts acute response to divalproex in mania. *Biol Psychiatry*. 1996;38:278.

...ost RM: Causes and mechanisms of bipolar illness onset and progression. In: Kowatch RA, Fristad MA, Findling RL, Post RM, eds. *A Clinical Manual for the Management of Bipolar Disorder in Children and Adolescents*. Washington, DC: APA Press, Inc., 2008:71.

...ost RM: Valproate use in psychiatry: A focus on bipolar illness. In: Loscher W, ed.: *Milestones in Drug Therapy. Valproate*. Basel: Birkhauser Verlag; 1999:167.

...ost RM, Leverich GS: *Treatment of Bipolar Illness: A Case Book for Clinicians and Patients*. New York: WW Norton; 2008.

...ost RM, Speer AM, Obrocea G, Leverich GL: Acute and prophylactic effects of anticonvulsants in bipolar depression. *Clin Neuroscience Res*. 2002;2:228.

...ao JS, Bazinet RP, Rapoport SL, Lee HJ: Chronic treatment of rats with sodium valproate downregulates frontal cortex NF-kappaB DNA binding activity and COX-2 mRNA. *Bipolar Disord*. 2007;9:513.

...agon NL, Altshuler LL, Fairbanks L, Elman S, Bitran J: Reproductive function and risk for PCOS in women treated for bipolar disorder. *Bipolar Disord*. 2005;7:146.

...agon N, Altshuler LL, Gudeman D, Burt VK, Tanavoli S: Medication status and polycystic ovary syndrome in women with bipolar disorder: A preliminary report. *J Clin Psychiatry*. 2000;61:173.

...aymond JR, Jamison KL, Bowden CL: Lamotrigine combined with divalproex or lithium for bipolar disorder: A case series. *CNS Spectr*. 2006;11:12.

...eichberg G: The mechanisms of action of valproate in neuropsychiatric disorders: Can we see the forest for the trees? *Cell Mol Life Sci*. 2007;64:2090.

...elsom JM, Cornelius JR, Daley DC, Kirisci L, Himmelhoch JM: Efficacy of valproate maintenance in patients with bipolar disorder and alcoholism. *Arch Gen Psychiatry*. 2005;62:37.

...ama RP, Rosen C, Kurian S, Guidotti A, Costa E: Valproic acid and chromatin remodeling in schizophrenia and bipolar disorder: Preliminary results from a clinical population. *Schizophr Res*. 2006;88:227.

...ata IS, Yatham LN, Baker GB: Divalproex sodium increases plasma GABA levels in healthy volunteers. *Int Clin Psychopharmacol*. 2000;15:221.

...ison D, Baker B, Chaplin W, Braun A, Hollander E: An open-label trial of divalproex extended-release in the treatment of borderline personality disorder. *CNS Spectr*. 2007;12:6.

...ue SC, Owens MJ, Lindsey KP, Knight DL, Nemeroff CB: Effects of sodium valproate on corticotropin-releasing factor systems in rat brain. *Neuropsychopharmacology*. 2001;24:624.

...ppen T, Kelly DL, Hynan LS, Snow DE, Sureddi S: Comparison of two anticonvulsants in a randomized, single-blind treatment of hypomanic symptoms in patients with bipolar disorder. *Aust N Z J Psychiatry*. 2007;41:397.

...ez AC, Bowden CL, Calabrese JR, Dilsaver SC, Morris DD: Pattern of response to divalproex, lithium, or placebo in four naturalistic subtypes of mania. *Neuropsychopharmacology*. 2002;26:530.

...ergall GS, Schneider LS, Mintzer JE, Cutler AJ, Cunningham MR: Safety and tolerability of divalproex sodium in the treatment of signs and symptoms of mania in elderly patients with dementia: Results of a double-blind, placebo-controlled trial. *Curr Ther Res*. 2001;62:51.

...ma SV, Ajaykumar B, Sindhu K, Nair MK, George B, Sarma PS: Motor and mental development of infants exposed to antiepileptic drugs in utero. *Epilepsy Behav*. 2008;13:229.

...ton M, Baker RW, Altshuler LL, Zarate CA, Suppes T: Olanzapine versus divalproex for the treatment of acute mania. *Am J Psychiatry*. 2002;159:1011.

...ton M, Baker RW, Altshuler L, Zarate CA, Suppes T: Olanzapine vs. divalproex sodium for bipolar mania: A 47-week study. Paper presented at: The Third European Stanley Foundation Conference on Bipolar Disorder; 2002. Freiburg, Germany.

...ton KD, Weller EB, Carlson GA, Sachs G, Biederman J: An open-label trial of divalproex in children and adolescents with bipolar disorder. *J Am Acad Child Adolesc Psychiatry*. 2002;41:1224.

...ue C, Frey BN, Andreazza AC, Cereser KM, Cacilhas AA: Effects of lithium and valproate on serum and hippocampal neurotrophin-3 levels in an animal model of mania. *J Psychiatr Res*. 2008;42(5):416.

...ton MF, DeGolia SG, Strong CM, Ketter TA: Divalproex therapy in medication-resistant bipolar II depression. *J Affect Disord*. 2001;67:207.

...ann S, Schmit J, Van Remoortel BA, Daelemans D, Este JA: Cell type-dependent inhibition of sodium valproate on human immunodeficiency virus type I replication in vitro. *J Acquir Immune Defic Syndr Hum Retroviruses*. 1997;13(2):187.

...ton CL, Vieta E, Young AH, Moller HJ, Paulsson B: A double-blind, randomized, placebo-controlled trial of quetiapine as an add-on therapy to lithium or divalproex for the treatment of bipolar mania. *Int Clin Psychopharmacol*. 2007;22:212.

...ton JV, Wissler R, Sachs G: A comparison of the efficacy, safety, and tolerability of risperidone and olanzapine in the treatment of bipolar disorder. *J Clin Psychiatry*. 2004;65:1114.

31.34 Brain Stimulation Methods

31.34a Electroconvulsive Therapy

JOAN PRUDIC, M.D.

HISTORICAL OVERVIEW

Convulsive therapies for major psychiatric illnesses predate the modern therapeutic era, with the use of camphor reported as early as the sixteenth century and the existence of several accounts of camphor convulsive therapies from the late 1700s to the mid 1800s. With the success of malarial fever therapy for general paresis, interest in biological therapies for psychiatric illnesses increased in the early twentieth century. By the 1930s, insulin coma and psychosurgery had also been introduced.

Unaware of the history of camphor convulsive therapy, the Hungarian neuropsychiatrist Ladislas von Meduna made the observation that the brains of epileptics had greater than normal numbers of glial cells, whereas those of schizophrenics had fewer, and he hypothesized that there might be a biological antagonism between convulsions and schizophrenia. Following animal experimentation, camphor was (again) selected as the appropriate agent to use for the therapeutic induction of seizures. In 1934, the first catatonic psychotic patient was successfully treated using intramuscular injections of camphor in oil to produce therapeutic seizures. Thirteen of a series of 26 patients treated similarly were reported to have had some degree of remission of psychosis. In 1937, a conference on convulsive therapies and insulin coma was held in Switzerland, and the use of these treatments spread.

Although effective, camphor was relatively long acting and was soon replaced by pentylenetetrazol. This agent was also associated with problems, principally patient rejection of the noxious sensations associated with γ-aminobutyric acid (GABA) antagonism while conscious—for example, increased heart rate, feelings of terror, and myoclonus preictally.

Lucio Bini and Ugo Cerletti were interested in the use of electricity to induce seizures, and, after a series of animal experiments and observation of the use of electricity commercially, they were able to safely apply current across the heads of animals for this purpose. In 1938, the first electroconvulsive treatment (ECT) course was administered to a delusional and incoherent patient, who improved with 1 treatment and remitted after 11. Electrical induction of convulsive therapy could be made more reliable and shorter acting than chemically induced convulsive therapies, and, by the early 1940s, had replaced them. In 1940, the first use of ECT occurred in the United States.

Throughout the 1940s, ECT was a first-line therapy, and efforts to improve its acceptability and safety profile continued in the ensuing decades. In 1940, A. E. Bennett developed the use of curare for the prevention of fractures that had previously resulted from the severe muscle contractions associated with the tonic phase of the seizure induction. By the 1950s brief general anesthesia with succinylcholine had replaced curare. Other improvements in anesthesia, most notably oxygenation throughout the treatment session, and cardiac and oxygen saturation monitoring became standard. Efficacy in disorders other than schizophrenia was demonstrated, most notably major depression.

In an effort to reduce the retrograde memory problems that persisted for some patients after the initial recovery period post ECT,

Table 31.34a–1 Milestones in the History of Convulsive Therapy

1500s	Paracelsus induces seizures by administering camphor (orally) to treat psychiatric illness.
1785	First published report of the use of seizure induction to treat mania, again using camphor.
1934	Von Meduna begins the modern era of convulsive therapy, using intramuscular injection of camphor for catatonic schizophrenia; camphor is soon replaced with pentylenetetrazol.
1938	Cerletti and Bini conduct the first electrical induction of a series of seizures in a catatonic patient and produce a successful treatment response.
1940	Electroconvulsive therapy (ECT) is introduced to the United States.
1951	A. E. Bennett develops curare for use as a muscle relaxant at ECT.
1958	Introduction of succinylcholine.
1960	First controlled study of unilateral ECT.
	Ottosson demonstrates that attenuation of seizure expression with an anticonvulsant agent (lidocaine) reduces the efficacy of ECT. In concert with other work suggesting that subconvulsive treatment produces only weak clinical responses, the hypothesis that seizure activity is both necessary and sufficient for efficacy is upheld.
1960s	Randomized clinical trials of the efficacy of ECT versus medications in the treatment of depression yield response rates significantly higher with ECT.
	Comparisons of neuroleptics and ECT show that neuroleptic medication is superior for acute treatment, although ECT may be more effective long term.
1970	D'Elia develops what has become the most common electrode positioning for right unilateral ECT.
1976	A constant-current, brief-pulse ECT device, the prototype for modern devices, is developed.
1978	The American Psychiatric Association publishes the first Task Force Report on ECT with the aim of establishing standards for consent and the technical and clinical aspects of the conduct of ECT.
Late 1970s to early 1980s	Randomized, controlled trials demonstrate that ECT is more effective than sham treatment for major depression.
1985	The National Institutes of Health/National Institute of Mental Health Consensus Conference on ECT endorses a role for the use of ECT and advocates research and national standards of practice.
1987	The belief that the seizure in itself is sufficient for clinical response is challenged by a report that the combination of dose just above the seizure threshold and right unilateral electrode placement, although producing a seizure of sufficient duration, is ineffective.
1988	Randomized, controlled clinical trials of ECT versus lithium demonstrate them to be equally effective in treating mania.
2000	In controlled trials, the dose–response relationship for right unilateral ECT is validated; high-dose right unilateral and bilateral ECT show equal response rates in major depression, but right unilateral electrode placement is associated with fewer adverse cognitive effects.
2001	Convulsive treatment is induced with magnetic stimulation by Lisanby and colleagues.
	The largest modern controlled trial of relapse prevention post-ECT with continuation pharmacotherapy demonstrates a significantly better outcome for combined treatment with a tricyclic antidepressant (nortriptyline) plus lithium compared to nortriptyline alone or placebo during the first 6 months post-ECT.
2006	In a large controlled trial, continuation ECT is demonstrated to be effective, but a fixed schedule is only equivalent to combination lithium/nortriptyline.
2008	Ultrabrief right unilateral ECT is shown to be equivalent to brief-pulse right unilateral and bilateral ECT in efficacy, but patients so treated are difficult to distinguish from a healthy, never-depressed control group in cognitive performance, including retrograde memory. In the same controlled trial, ultrabrief bilateral ECT at 150% above the seizure threshold was ineffective, confirming earlier observations that the seizure itself is not sufficient for efficacy.

explorations of nondominant electrode placement and alternative, more efficient waveforms were undertaken in subsequent decades. The practice of ECT also benefited from the introduction of controlled trials methodology, which demonstrated its safety and efficacy, and from refinements made in diagnostic systems and the process of informed consent. In the 1980s and 1990s efforts to assure uniformly high standards of practice were underway with the publication of recommendations for treatment delivery, education, and training by professional organizations in the United States, England, Scandinavia, and Canada, among others.

With the widespread use of pharmacological agents as first-line treatments for major psychiatric disorders, ECT is now more commonly used for patients with resistance to those treatments, except in the case of life-threatening illness due to inanition, severe suicidal symptoms, or catatonia. Although the failure of subconvulsive stimulation to induce the remission of psychiatric illness and the effectiveness of chemical convulsive therapy suggested that the seizure was necessary and sufficient for therapeutic benefit with ECT, it is now known that there is a dose–response relationship with right unilateral ECT and that bilateral ECT is likely to be ineffective with ultrabrief pulse widths. Work continues to explore the underlying mechanisms and biological characteristics of effective ECT treatments, with interest in having the treatment focus on appropriate neural networks with a more efficient stimulus as a method of reducing cognitive side effects. With the growing understanding that depression is a chronic disease for many patients, more emphasis has been placed on continuation and maintenance treatments following an acute course of ECT. Work has been published demonstrating the efficacy of both psychotropics and ECT in reducing relapse post ECT.

Utilization of ECT has diminished since the middle of the twentieth century; but because ECT remains the most effective treatment for major depression and a rapidly effective treatment for life-threatening psychiatric conditions, ECT, unlike its contemporaneous somatic therapies, such as insulin coma, remains in the active treatment portfolio of modern therapeutics. Its use has shifted from public to private institutions, and it is estimated that approximately 100,000 patients have received ECT annually over the last few decades in the United States (Table 31.34a–1).

ELECTRICAL INDUCTION OF SEIZURES

Factors in the Generation and Measurement of Electrical Stimulation for ECT

ECT is a form of brain stimulation in which induction of a seizure occurs when an applied electrical stimulus creates an electrical field

with flow of current in the excitable tissue of the brain sufficient to depolarize cell membranes of neurons synchronously. Fundamentally, the generation and behavior of the electrical stimulus can be conceptualized in terms of Ohm's law: V (voltage) $= I$ (current) $\times R$ (resistance). Here, voltage is the electromotor force (measured in volts) causing current to flow; current is the rate of flow of electrons (in amperes); and resistance is the relative ability to pass current (in ohms). Ohm's law assumes a direct current (DC) circuit, but ECT devices function on alternating current. In this situation, it is necessary to replace the resistance with the impedance (Z). Impedance involves capacitance and inductance, as well as resistance. Because biological tissues are nonferrous and thus have low inductive properties, the inductance term is usually assumed to make little contribution to the impedance during ECT. Capacitance (F) is the ability to store charge (in farads). Neural tissue has relatively low capacitance (10^{-12} to 10^{-10} F), and the electrode–skin interface (estimated 0.4 μF) is the source of a relatively greater contribution to this term.

Although it is possible to trigger a seizure with a single DC pulse of long duration, voltage and current may vary over time in the electrical stimulus as clinically used. A variety of stimulus waveforms has also been used to deliver the stimulus, including sine wave, rectified partial sine wave, brief-pulse square wave, and ultrabrief-pulse square wave. These different waveforms are not of equal efficiency in depolarizing neural tissue. By examining mammalian neurons, it has become evident that fast-rising current results in firing at lower current intensity and, hence, lower dose. The slow rise of a sine wave results in accommodation and increases in the threshold for neuronal firing. This observation has led to a preference for brief-pulse waveforms that "instantly" achieve peak intensity (on the order of microseconds) over the relatively slower-rising sine waveform, which typically reaches peak intensity in several milliseconds.

Chronaxie, and hence optimal pulse duration, for human neuronal tissue is on the order of 0.1 to 0.2 ms. Furthermore, once nerves have fired, they enter a refractory period, and continued stimulation will not elicit further response. This has led to a reexamination of the need for longer-duration stimulation per phase where much of the stimulus is delivered when the neuronal tissue is refractory. Even brief-pulse waveforms with pulse widths on the order of 0.5–1.2 ms, commonly used in modern devices, may be expected to deliver excessive energy in the refractory period, although it is an order of magnitude lower than with sine wave stimulation. Finally, it has been observed that increasing the frequency of pulses is less efficient in eliciting depolarization than increasing the train duration of pulses when using a brief-pulse device. This phenomenon is probably also related to the inefficiency of stimulating tissue during the neuronal refractory period.

Once the electrical stimulus is generated, current is distributed inversely to the resistance of the tissue compartments traversed. There are three major components: Scalp (about 200 ohms), skull (about 18,000 ohms), and brain tissue (about 200 ohms). Because current flow is greatest across the lowest resistance, it has been estimated that 80 percent of current is shunted through the scalp. The skull obviously provides the greatest component of resistance, and skull anatomy—for example, the position and size of sutures, thickness, and so on—greatly affects the proportion of remaining electrical dose that enters brain tissue. Differences in scalp and skull anatomy are thought to be the major source of the wide variation among individuals in the electrical dose required to elicit a generalized seizure or seizure threshold. These differences have been observed to be of the order of 100- to 200-fold.

Another influence on current shunting is interelectrode distance: The closer the electrodes are placed on the skull, the more shunting occurs. It is thought that right unilateral placements can result in the creation of a virtual electrode occurring in the area between the two electrodes and, hence, in reduced amounts of electrical dose required for seizure elicitation. This increased shunting may also result in lower current density in brain tissue.

There is a tradition of expressing the quantity of the electrical stimulus delivered as energy (measured in joules) or, in the modern era, as charge (in millicoulombs). Substantial evidence indicates that current density in neural tissue is the critical factor responsible for seizure production and the subsequent neurobiological effects of the electrical stimulation. Although it is not now possible to measure charge density directly in human neural tissue during ECT, dynamic impedance could be used to approximate charge density because of its relationship to current shunting during stimulus delivery. When electrode site preparation and positioning are standardized, anatomic factors become the major determinants of impedance. If these factors are also constant during the treatment, impedance can then reflect current density in brain tissue.

With the development of other forms of electrical and also magnetic brain stimulation, there has been revived interest in understanding and exploring the effect of electrical stimulation on brain tissue. The various elements of the brain have differing electrical properties and vary markedly in excitability, with myelinated axons being most excitable and neuronal cell bodies and dendrites least. Tissue response also varies with distance from electrical source—in this case, the stimulating electrode. Although direct recording of the effects of electrical stimulation is not available for ECT except in animal models, functional neuroimaging and computational modeling are expected to expand our understanding of the physiology of the treatment.

Devices Used to Deliver ECT

Although constant-current, constant-voltage, and constant-energy devices have been in use, most modern instruments are constant-current devices because constant-voltage devices have become outmoded. The range of constant current is on the order of 0.5 to 1 A in these devices. Dose is manipulated by varying the time of exposure to a fixed current (total charge). With brief-pulse devices—the most commonly used constant-current devices—frequency of pulses, pulse width, and duration of pulse train are parameters that can be used to vary the stimulus dose. Because impedance varies directly with voltage, particular attention must be paid to impedance in a constant-current environment. Commonly, impedance is tested prior to stimulus delivery by passage of a low-amplitude, high-frequency test stimulus. If impedance exceeds manufacturer limits, treatment stimuli are not permitted by the device, although some devices are equipped with override features. If too high, impedance is usually lowered by improving skin electrode contact, although other parts of the circuit may also need examination and adjustment. By keeping impedance within safe guidelines, local tissue damage is avoided. When impedance is too low, voltage will also be very low and might not be sufficient to drive enough current flow to brain tissue, where the resulting charge density may not be great enough to cause synchronous neuronal depolarization and the desired biological effects. Low impedance is usually the result of current shunting in the scalp and is corrected by interrupting any alternative current pathway at the skin surface—for example, saline used to prepare the electrode site that runs together and forms a continuous pathway at the scalp.

Calculation of stimulus energy in joules requires information about interelectrode impedance, which is not readily available. Charge is commonly used to measure the intensity of the stimulus used in treatment with brief-pulse devices. Charge is the quantity of electrons flowing through a conductor over a given time period (in coulombs) and can easily be computed from the parameters of a brief-pulse, constant-current device.

Constant-voltage devices allow current to vary inversely with impedance. The typical device generates a sine wave stimulus and has a range of 70 to 170 V. With these devices, high impedance will result in low current flow, which in turn, theoretically, may be inadequate to induce sufficient charge in neuronal tissue to result in neuronal depolarization. Because the practitioner does not have access to crucial information about impedance when using a constant-voltage device, it may be difficult to assess current intensity in this setting, and judgments about the adequacy of parameters can be difficult to make. The use of these devices in the United States has become outmoded.

ECT device output in the United States has been capped at 100 J, which corresponds to a charge of 500 to 600 mC, depending on the particular device specifications. With ultrabrief pulse width, this range is adequate to deliver right unilateral ECT to most patients. ECT devices in the European Union and

elsewhere can have an extended range up to 200 J to allow delivery of adequate dose with brief-pulse right unilateral electrode placement, which is mandated in some EU nations.

MECHANISMS OF ACTION

The relative inaccessibility of the central nervous system has made understanding the pathophysiology of psychiatric diseases a continually evolving process. As a consequence, the mechanisms of action of ECT, the oldest somatic treatment currently in use in the field of psychiatry, continue to be an active area of hypothesis and research. Past and present theories abound, and a wide range of data, particularly at the preclinical level, are available on the effects of electroconvulsive stimulation.

Proposed mechanisms have involved theories in almost every domain. These include psychological constructs: structural explanations—of latest interest, neural plasticity; interpretations based on electrophysiology and neurophysiology; biochemical theories encompassing neurochemistry, including neuroendocrine phenomena; and other molecular rationales, including genetic mechanisms and second messenger systems.

Among psychological theories, there is no evidence that fear, regression, or increased medical attention account for the efficacy or side effects of ECT. Because many of the most recent advances in the field have reduced the adverse cognitive effects of ECT while maintaining efficacy, there is little reason to believe that memory loss has much mechanistic validity. Extensive reviews of the preclinical and clinical literature have refuted the assertion that brain damage occurs, let alone accounts for ECT's effects. Furthermore, current anesthesia practice assures that hypoxia does not occur. Sham ECT (anesthesia alone) is ineffective; hence, anesthesia is unlikely to play a role in the mechanism of action.

Distinguishing the relevance of observed phenomena with electroconvulsive stimulation constitutes a major challenge in the area of mechanisms. Considerations include questions about the relevance of animal data, much of which has been derived from rodents, although there has been recent interest in primate work. This work suffers from the lack of adequate animal models of the psychiatric syndromes for which ECT is used. In preclinical work, electroconvulsive stimulation is often given in a time course that does not closely follow the treatment course given to patients, that is, two to three times weekly. For example, stimulation is administered once or several times in one day in preclinical investigations.

ECT has a very broad spectrum of efficacy and action, as will become evident from discussions of indications for its use, of efficacy in a variety of syndromes, and of its side effects. The treatment is often studied in comparison with antidepressants or, to a lesser degree, other psychotropics. It is known that there is overlap in mechanistic effects, but ECT has more therapeutic effects than any studied medication. Coupled with the fact that ECT has more indications for treatment, the challenge of ascertaining critical similarities and differences is significant. Because of the perceived invasiveness of the treatment, the usual severity of illness among treated patients, and the necessity for anesthesia, little work is being done with sham ECT. There are limited data available from weaker forms of the treatment—for example, right unilateral ECT at low or modest dose or ultrabrief bilateral ECT, which are known to be a less effective form of the treatment.

Biochemical Actions

There is a substantial body of work comparing electroconvulsive stimulation with psychotropic (and other) medications whose actions and mechanisms have been assayed in vitro and in vivo, most often preclinically, but also in human studies. Not surprisingly, the major areas of interest have been in neurotransmitter and peptidergic systems. The primary focus has been on monoamine effects, many of which are shared by ECS in animals, ECT in humans, and psychotropics, especially antidepressants. Although it appears that both electroconvulsive stimulation and antidepressants downregulate β-adrenergic receptors, human studies of broader changes in noradrenergic pathways have been characterized by inconsistent outcomes. There are also various data on the effects of antidepressants and ECT on serotonergic systems: Antidepressants typically downregulate 5-hydroxytryptamine receptors (5-HT_2), whereas ECT leads to increased density of 5-HT receptors (in rodents) and decreased binding (in primates). Although serotonergic transmission may be enhanced by both antidepressants and ECT, the mechanisms appear distinct. ECT is more effective than antidepressant medications, so that defining what possible mechanisms are responsible for this phenomenon are of pharmaceutical as well as heuristic interest. The critical differences are not known. Both animal and clinical studies indicate increased dopaminergic function following electroconvulsive stimulation, particularly D_1 and D_2 receptor function. Although this effect may be an underlying mechanism for ECT's therapeutic effects in Parkinson's disease, it does not help to clarify the underlying process for the benefits conferred by ECT on patients with schizophrenia and other psychotic illnesses, in which dopaminergic antagonism, at least in some brain regions, has been presumed to be critical.

Another major area of interest has been the variety of different neurotransmitter systems that might form the biochemical foundation for the anticonvulsant effects of electroconvulsive stimulation. Because of the efficacy of anticonvulsant medications in mania, there is also speculation that the anticonvulsant effects of ECT contribute to its efficacy in mania. Most of this work is preclinical and indicates mixed GABAergic activity, upregulation of adenosine receptors, and blocking of anticonvulsant effects with opiate antagonists. GABAergic effects in humans are being explored neurophysiologically. It has been difficult to duplicate anticonvulsant effects of opiate antagonists in humans. The proconvulsant effects of caffeine, aminophylline, and similar compounds are observable in humans and are thought to be due at least in part to alterations in adenosine transmission, even though these agents have other biochemical effects that might also contribute. Investigations into possible glutaminergic mechanisms, particularly their relationship to cognitive effects, are underway. Unfortunately, it is not currently possible to conclude that alterations in any transmitter system are associated with the efficacy of ECT in any syndromic for which it is used.

Most recent preclinical research focuses on growth factors and molecular mechanisms. It appears that brain-derived neurotrophic factor and nerve growth factor are both increased by a single electroconvulsive stimulus (ECS) and chronic ECS, whereas neurotrophin is decreased. There is interest in linking these observations to those made of marked neural plasticity in some brain areas—for example, hippocampus—due to ECS. Work continues with a wide variety of other neuropeptides, such as somatostatin, cholecystokinin, precursors of opiates and thyroid hormones, and so on. Other areas of interest concern the effects of ECS on second messenger systems, genetic expression, and transcription regulation. The work, focused largely on molecular phenomena related to cell proliferation—both neuronal and vascular—plasticity and resiliency, including antiapoptotic effects, is expanding steadily, but its clinical and functional significance remains to be defined.

Hypotheses related to neuroendocrine mechanisms were generated early in the history of the use of ECT. Most hypotheses reason that stimulation of diencephalic structures, especially the hypothalamus, is involved and perhaps critical to the efficacy of the treatment. Experimental designs generated by these hypotheses have involved indirect quantification of function, specifically various peripheral neuroendocrine measures. Examples include corticotropin-releasing hormone, adrenocorticotropin, and cortisol. Con-

...and subacutely; studies of oxytocin and vasopressin; and measures related to growth and thyroid hormones. There is no consistent evidence that acute or subacute changes in neuroendocrine factors affect efficacy or cognitive ...

Neurophysiology

With advances in the area of brain imaging, neurophysiology has become a focus of interest in investigating the mechanisms of action of ECT. It is known that large increases in global cerebral blood flow (CBF) and cerebral metabolic rate (CMR) occur along with increased blood–brain barrier permeability during generalized seizures, including those electrically induced. In the postictal period there is functional suppression, with decreases in CBF and CMR, as well as varying degrees of bioelectric suppression on EEG. Changes are also topographically distributed. These reductions have been correlated with treatment outcome.

The magnitude of reductions in CBF in specific prefrontal regions is related to the efficacy of ECT, and responders are more likely to exhibit postictal suppression and develop slow wave activity on EEG than nonresponders. As techniques have been refined, the possibility of identifying specific functional networks and associating them with efficacy has improved. Related work has yielded information concerning the way seizures are generated with various electrode placement and electrical dosing techniques. For example, studies comparing efficacious forms of bifrontotemporal, bifrontal, and right unilateral electrode placements indicate that the prefrontal cortex, particularly on the right, the anterior cingulum, and associated subcortical areas, including the right medial thalamus, brainstem, and midbrain tegmentum, are involved. Ineffective forms of ECT—for example, low-dose right unilateral—trigger seizures from the motor cortex and involve the prefrontal area less. Investigations involving deep brain stimulation point to these areas as well, particularly Brodmann's area 25, the anterior cingulum, and the thalamus. These observations are important to clarifying which brain regions are critical to the efficacy of the treatment, as well as to understanding the dose–response relationship of electrical stimulation above seizure threshold to efficacy that has been observed for right unilateral ECT. There also has been expanding work using brain imaging technologies to investigate networks related to the cognitive effects of the treatment. Although preliminary, this work confirms the involvement of the medial temporal lobe in anterograde amnesia and points to prefrontal cortex involvement in retrograde amnesia.

Although neurophysiologic inquiries are continuing, they are hindered by the limited localizing value and coarse resolution of available methods. The degree of covariance among various regions and the spatial distribution and magnitude of association are yet to be defined. There is also a need to better characterize topographies and to determine whether normalization, abnormalization, or independence observations applies. In addition, investigational samples are small and heterogeneous.

Neuroplasticity

Recently, there has been increased interest in structural changes in the brain associated with psychiatric syndromes and response to treatment. This has been particularly so for microscopic changes associated with electroconvulsive stimulation, as well as antidepressant and other medications. In animals, mostly rodents, synaptic plasticity in hippocampus, including mossy fiber sprouting, alterations in synaptic structure, increased connectivity in perforant pathways, and promotion of neurogenesis, and the suppression of apoptosis have been observed. Many of these structural events are also observed, although to a lesser extent, with antidepressant medications such as fluoxetine. These reports have also galvanized controversy over various aspects of the technical validity of the observations. It is unknown whether such changes occur clinically and, if they do, what significance to efficacy and cognitive side effects might be discovered.

INDICATIONS

Although, historically, the first diagnostic indication for ECT was schizophrenia, practice has evolved in the last 65 years. Approximately 85 percent of patients currently receiving ECT in the United States have major depression as the diagnostic indication for its use. The remainder have schizoaffective disorders, mania, and schizophrenia, with a few other diagnoses such as Parkinson's disease completing the inventory of indications. The clinical literature demonstrating the short-term efficacy of ECT in the major syndromes for which it is used is considerable and includes randomized, controlled trials with sham treatment or with medications as alternatives, outcome data from studies involving various treatment techniques, and uncontrolled data and surveys of expert opinion.

Beyond diagnostic indications, there are other clinical considerations commonly brought to bear in the prescription of ECT. Historically, ECT was a first-line treatment for the major psychiatric syndromes, but with the development of psychopharmacological treatments, use as a primary treatment has decreased, and resistance to medications has become the most common clinical indication. Nonetheless, when patients require rapid clinical response because of the severity and danger of psychiatric symptoms or medical problems resulting from psychiatric causes, ECT may be given without a prior drug trial. Other situations are when there has been prior optimal response with ECT or the patient prefers the treatment over medications (Table 31.34a–2).

Mood Disorders

Major Depression. ECT is the most effective treatment for major depression. It is commonly used as the standard against which other treatments, including innovative treatments such as repetitive

Table 31.34a–2. Indications for the Use of Electroconvulsive Therapy (ECT)

Diagnoses for which ECT may be indicated
Major diagnostic indications
Major depression, both unipolar and bipolar
Psychotic depression in particular
Mania, including mixed episodes
Schizophrenia with acute exacerbation
Catatonic subtype particularly
Schizoaffective disorder
Other diagnostic indications
Parkinson's disease
Neuroleptic malignant disorder
Clinical indications
Primary use
Rapid definitive response required on medical or psychiatric grounds
Risks of alternative treatments outweigh benefits
Past history of poor response to psychotropics or good response to ECT
Patient preference
Secondary use
Failure to respond to pharmacotherapy in the current episode
Intolerance of pharmacotherapy in the current episode
Rapid definitive response necessitated by deterioration of the patient's condition

transcranial magnetic stimulation, are compared. No treatment has been found to be superior to ECT in the treatment of major depression in a controlled trial.

Evidence for ECT's efficacy derives from several different sources. The introduction of the treatment occurred prior to the development of clinical trials methodology in the post–World War II era. In the 1940s, open clinical series and case studies cited response rates of 80 to 90 percent with the use of ECT as a first-line treatment. Decreased chronicity of illness, decreased morbidity, and the suggestion of decreased mortality were frequently cited as benefits of ECT. From the 1950s through the 1980s, ECT was subjected to randomized clinical trials with sham ECT and psychotropic medications as comparators. In the sham versus real ECT trials, anesthesia alone was used for comparison groups because of a concern that there were benefits from its repeated use. ECT was shown to be consistently superior, and the further use of sham conditions has been abandoned in studies of major depression. From the 1950s onward, there has also been interest in the relative efficacy of antidepressants and ECT. In these reports ECT has been found to be 20 to 40 percent more effective than medications, and there has not been a study that found medication to be superior to ECT. Most of this work was conducted in the earlier decades of this period and was limited by the possibility that modern pharmacological standards would dictate more aggressive dose and duration of treatment in the medication conditions. In this type of study, adequate blinding is not possible, and concerns about bias cannot be completely dispelled even if clinical raters do not know the treatment conditions. Many of the antidepressants investigated in the past have been superseded by newer compounds, such as the specific serotonin reuptake inhibitors and pharmacologically unique agents such as bupropion and mirtazapine. Unfortunately, there is little data to inform comparisons of ECT and modern pharmaceuticals.

Although in an earlier era prior to modern advances in defining the phenomenology of depression it was thought that various clinical criteria conferred a negative prognosis to the use of ECT, more recent observations have found ECT to be effective for all subtypes of major depression, including unipolar and bipolar depression, melancholia, and psychotic depression. There have been suggestive data that psychotically depressed patients have a superior response to ECT, whereas there is suboptimal response with antidepressants alone, and the recommended regimens of adequate doses of both an antidepressant and an antipsychotic are seldom given, perhaps due to poor tolerance of the combination. ECT may be particularly useful for psychotically depressed patients because the syndrome is often accompanied by severe symptoms and greater risk of suicide.

ECT can also be used safely in all populations of patients, including those often considered to be at special risk: The elderly, the medically ill, pregnant women, and adolescents. Each of these groups may require specific considerations and extra preparation and/or precautions to be taken prior to treatment. ECT has even been used to treat preadolescent children, although rarely.

Dilemmas persist among experts in the field about when to offer ECT in the course of treatment for major depression. The hierarchy of factors that need to be considered has not been resolved, but it is important to gauge the risk of not terminating an episode of depression while giving sequential trials of antidepressants along with augmentation and combination medications versus the risk of the principal side effects of ECT, namely persistent retrograde memory deficits of varying significance. With recent improvements in technique, these cognitive effects have been reduced to the point where, in at least one study, they were difficult to detect. Even with these improvements, an acute course of ECT will often disrupt the routines of daily life because of the recovery requirements accompanying general anesthesia. Another important consideration relates to the fact that major depression is a subacute and often chronic disease with a need for continuation and maintenance treatment. For ECT, acute response is followed by the need to determine adequate maintenance treatment, most often pharmacological, although maintenance ECT is also an option. This circumstance can also affect the timing of the choice of ECT versus pharmacology.

Finally, the response rates cited early in the history of ECT must be adjusted to the changing makeup of patient populations receiving the treatment. It appears that prior medication nonresponse, length of an episode, extended lengths of episode, and comorbidity with other psychiatric conditions may lower the expected response rate. Comorbidity with personality disorder that may independently contribute to mood changes can be especially problematic because patients with personality disorder can also suffer major depression, and it is difficult to define what phenomenology belongs to each syndrome and to determine expectations. This does not automatically mean that ECT should be withheld from these populations. Response rates to alternative treatments may be even lower, whereas response to ECT in antidepressant nonresponders can be expected to be 50 to 70 percent.

Mania; Mixed States and Rapid Cycling. Historically, ECT was a first-line treatment for mania as well, but pharmacological strategies, particularly lithium, anticonvulsants, and atypical neuroleptics, have become the mainstay of treatment for the manic episodes. In the modern era, the use of ECT is generally reserved for patients who are resistant or intolerant to the usual medication treatments, including those with mixed states or rapid cycling, or who have very severe symptomatology, for example, manic delirium. Organizations issuing guidelines for the use of ECT to treat mania have assigned it to second-line status (World Federation of Societies of Biological Psychiatry; American Psychiatric Association [APA]; Canadian Network for Mood and Anxiety Treatments) or third-line status (National Institute for Clinical Excellence) for acute episodes, only the APA recommends its use as a maintenance treatment for bipolar disorder.

Compilations of the evidence for the use of ECT in mania have reported 75 to 80 percent response rates. The bulk of the evidence comprises uncontrolled case series, undoubtedly because of the great difficulty in conducting usual clinical trials in this population due to uncontrolled behavior, difficulties in assuring capacity to consent, and so on. The only sham versus real ECT study with patients on neuroleptics in both conditions demonstrated superior outcomes for ECT patients both in response rates and in lower neuroleptic requirements. Controlled retrospective comparisons have found ECT to be equivalent to lithium and at least as efficacious as typical neuroleptics, if not more so. Prospective work demonstrated equivalence to lithium in studies in which all patients received neuroleptics as well as the study treatments: One small study comparing ECT to lithium and neuroleptic in patients who failed lithium or neuroleptic found ECT to be noticeably superior to combined pharmacology. There have been no comparisons of ECT to anticonvulsants. Early work that suggested the need for increased frequency in treatment schedule and increased numbers of sessions to complete a treatment course has not been borne out in modern studies, which have used standard treatment schedules.

A prospective trial and a retrospective controlled review have found that patients in mixed states are responsive to ECT, although increased numbers of treatments may be required compared to pure manic or depressed states. Case reports have indicated that ECT is also potentially effective in managing rapid cycling, in which finding effective pharmacological approaches can be particularly complex and difficult. Response rates are lower than for acute manic states.

Schizophrenia

Although schizophrenia is the second-most-common diagnostic indication for ECT, there is a lack of expert consensus about its use and wide disparity in practice. This may be due to the current understanding of schizophrenia as a chronic illness and to the scarcity of evidence supporting the efficacy of ECT for chronic symptoms. Especially since the advent of atypical antipsychotic medications, pharmacological treatment remains the first choice.

ECT was introduced for use in schizophrenia, and the earliest reports, consisting of case series and comparisons with historical controls and nonsomatic treatments, were quite positive. As with other observations from this era, there was a lack of scientific methodology in diagnostic and outcome criteria, which would not conform to modern standards. Real versus sham ECT studies were carried out with chronic patients in the 1950s to 1960s and on more acutely ill patients on neuroleptics in the 1980s. The earlier studies showed no advantage for ECT over anesthesia, but the later studies showed ECT to be superior to anesthesia alone. The source of the disparate outcomes is unclear, but, in addition to differences in chronicity, the presence of neuroleptics in the modern samples may be critical. Because of the positive reports of efficacy in the first decades of use, ECT was also used as the standard against which to compare newer somatic therapies, particularly neuroleptics when they were first introduced. Although subject to the usual limitations of such early clinical trials, it soon became apparent that, at best, ECT was equivalent to neuroleptics in short-term efficacy. At this point, pharmacology superseded ECT for the treatment of schizophrenia. One observation from this era has remained intriguing and might merit further consideration. In one-term follow-up, patients who had received ECT had superior outcomes.

Equal attention has been paid to examining the combination of ECT with neuroleptics versus treatment with either modality alone. The combination treatment is generally superior to monotherapies, but the evidence for such observations is considered to be less than definitive due to relatively small samples and disparity in methodology among the studies. It appears that lower doses of neuroleptic are needed in combination treatments. A recent study of combination treatment versus monotherapy in maintenance treatment of schizophrenia again showed promise, particularly in the first weeks of treatment. Although few of these studies reached full standards for a clinical trial, lack of random assignment and full blinding, there is a suggestion that ECT may be useful for treatment-resistant patients and those who easily relapse on monotherapy. Thus far, most of the published observations on the use of ECT in schizophrenics resistant to neuroleptics are somewhat impressionistic as well. Recent reports confirm the safety of using ECT and atypical antipsychotics, with clozapine as the oldest and most reported agent. Most professional bodies issuing guidelines for the treatment of schizophrenia reserve ECT for patients who are nonresponsive or intolerant to clozapine.

Because ECT does not have a broader therapeutic spectrum than neuroleptics, it is not surprising that patients with good prognosis for pharmacological treatment are also those that do best with ECT. Evidence to support the traditional view that the presence of affective symptoms improves the likelihood of response to ECT is inconsistent, and there is no controlled evidence concerning the use for schizoaffective patients. Uncontrolled observational evidence supports the efficacy of ECT in schizoaffective illness, but response falls short of that obtained in straightforward affective disorder.

One last area of interest is the effect of ECT on the movement disorders resulting from neuroleptic treatment of schizophrenia. Extrapyramidal symptoms induced by neuroleptics are reversible by pharmacological intervention and respond to ECT. Furthermore, there is evidence from several case reports that ECT may protect against the development of tardive dyskinesia in neuroleptic-treated patients. This observation is consistent with preclinical observations of the effects of ECS on the dopaminergic system and the effects of ECT on patients with Parkinson's disease.

Other Diagnostic Indications

In general, ECT treatment for other indications is supported by case material only. The use of ECT will be rare and only when standard treatments cannot be tolerated or fail.

Psychiatric. There is only very limited information about the effect of ECT on other *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV), Axis I disorders and no evidence for clinically significant efficacy without the presence of another primary diagnostic indication. There has been interest in anxiety disorders because of the overlap in symptomatology and pharmacological therapeutics between affective and anxiety disorders, but the only published data concern obsessive-compulsive disorder (OCD). Prospective work demonstrated acute response in OCD, but patients soon relapsed, and ECT is not recommended for this disorder. Because of the not infrequent presence of symptoms of panic in depressed patients undergoing ECT, the question of the effect of the treatment on these symptoms should be raised, but there are no studies of the effect of ECT on panic disorder. Even though dysthymia is on the spectrum with major depression, there is no demonstrated efficacy. Patients with double depression (dysthymia and major depression) have similar response rates to those with episodic major depression alone but are left with higher levels of mild depressive symptoms at the end of treatment, suggesting that dysthymia is more difficult to ameliorate with ECT even in the setting of comorbid major depression. The delirium that can accompany withdrawal and toxic states induced by some substances, such as alcohol and phencyclidine, can be treated with ECT, but the underlying substance abuse syndrome is not significantly affected. This use of ECT is largely of theoretical interest.

Another area of concern is the issue of comorbidity with personality disorders. Here most of the work concerns Cluster B disorders, especially borderline personality disorder. A secondary area of interest should be Cluster A disorders because of their hypothesized overlap with Axis I anxiety disorders. In general, comorbidity with one or more personality disorders is associated with poorer outcomes, especially higher relapse rates. The challenge for clinicians is to discriminate between affective symptoms that result from the personality disorder and those that constitute an ongoing affective episode. ECT is not considered to be a treatment for any personality disorder.

Neurological. ECT has been used rarely for the treatment of several neurological disorders, usually in situations in which they are comorbid with a psychiatric disorder that is an indication for ECT. The most common of these is catatonia, a syndrome characterized by stupor, mutism, and a variety of motor symptoms, including posturing, waxy flexibility, and catalepsy. Schizophrenia and bipolar disorder are the most frequent underlying diagnoses. Benzodiazepines are the primary treatment for catatonia along with a primary pharmacological approach to the comorbid psychiatric disorder. When catatonia is resistant, ECT may be used. The data supporting this approach are largely uncontrolled but quite positive. The syndrome of lethal catatonia is characterized by stupor or excitement, hyperthermia, autonomic dysregulation, rigidity, and changes in consciousness. ECT can be quite effective and, in fact, life saving. Neuroleptic malignant syndrome is an iatrogenically induced form of lethal catatonia and is often treated with dopaminergic strategies, as well as with sedatives. Outcomes with ECT are equivalent to those obtained pharmacologically, but ECT has the advantage of being a treatment for the comorbid psychiatric syndrome for which neuroleptics must be discontinued. There is evidence that neuroleptic malignant syndrome (NMS) is less frequent with atypical antipsychotics, and the use of ECT for NMS may become less necessary as practice changes.

Open and sham-controlled data have demonstrated that the motor symptoms of Parkinson's disease, especially rigidity and bradykinesia, are lessened by ECT, particularly in the "off" phase of treatment that characterizes the phase of the disease treated with L-dopa. These effects are of 4- to 6-weeks' duration generally, but there are reports that maintenance ECT may be helpful as well. ECT is seldom used as a primary treatment for Parkinson's disease, and it is more frequently used to treat the comorbid depression that can occur with the disorder. The combination of ECT with levodopa/carbidopa may require decreasing medication dose to stave off dyskinesia or delirium as complications

of combined treatment. With the increasing use of Clozaril and other atypical neuroleptics to manage the side effects of levodopa/carbidopa, the use of ECT for Parkinson's disease has diminished.

The anticonvulsant effects of ECT are well characterized, and ECT has been used in epilepsy, although effects are time limited, and ECT has no demonstrated superiority over anticonvulsant medications. When such patients are treated, including when they are treated for comorbid psychiatric conditions more commonly treated with ECT, the dose of anticonvulsant medications is usually not changed, except when therapeutic seizures cannot be elicited. Theoretically, ECT might be of use in intractable seizures or status epilepticus.

There are reports of lessening of pain syndromes when comorbid depression is treated with ECT. ECT has also been used to mitigate other movement disorders—for example, Tourette's syndrome. Historically, there have been cases of delirium of both medical and psychiatric cause that respond to ECT, although the treatment is very, very seldom used for this reason currently.

The remainder of ECT use in neurological syndromes is as treatment for comorbid affective and, less commonly, psychotic syndromes. There are case reports and series of its use in poststroke depression and mood disorders accompanying dementia, mental retardation, and even head trauma and brain tumors. In all of these diagnoses, the risk of cognitive side effects of ECT can be greater, and modifications of the treatment may be needed, for example, to avoid skull defects found with trauma or to minimize the ictal blood pressure changes for patients with modest, stable brain tumors.

PATIENT MANAGEMENT

Pretreatment Evaluation

Evaluation of patients for treatment with ECT should be done as close to the first treatment session as possible. Both psychiatric and medical assessments are needed to conduct a risk–benefit analysis for the treatment of an individual patient. The psychiatric component of the pretreatment evaluation is generally conducted by a practitioner privileged to administer ECT, but there are often contributions from the patient's attending psychiatrist if different from the ECT provider. Establishing the indications for ECT include a careful diagnosis, as well as consideration of other clinical factors contributing to the recommendation for ECT, such as severe suicidal risk. There may be local requirements and regulations for second opinions, especially in special populations such as adolescents and children.

Past treatment with ECT should be explored not only for response, but also to identify technical aspects and tolerance of the treatment. Knowledge of prior ECT treatments will guide recommendations for the current course. Pharmacological treatments should be evaluated for number, adequacy, tolerance, and degree of response. Psychotropic history can be an indication for ECT, as well as a basis for recommendations concerning post-ECT continuation treatment. Decisions regarding the adjustment of psychotropic medications should be based on the degree to which they may enhance response (e.g., maintaining an antipsychotic), the possibility that they may interfere with ECT (e.g., anticonvulsants used as psychotropics), the possibility that medications may contribute to adverse effects (e.g., lithium), and the need to maintain medications for patient management while ECT takes effect.

As part of the pretreatment evaluation there should be documentation of the target symptoms to facilitate evaluations during the treatment course and decisions concerning the termination of acute treatment. In addition to behavioral assessments, cognitive evaluation pretreatment is also critical. At a minimum, those aspects of cognitive function most likely to be affected should be documented at baseline: Orientation and memory, including recall of recent and remote events. Evaluation of language and visual motor and perceptual abilities can also be valuable. Finally, patients' subjective assessment of their cognitive and memory functioning should also be documented, particularly given that the predominant diagnostic indication for ECT—depression—is often accompanied by both subjective and objective memory problems.

The medical component of the pre-ECT evaluation focuses on a patient's ability to tolerate anesthesia along with ECT and should be conducted by an ECT practitioner and an anesthetist. The scope of medical evaluation is similar to that conducted for patients undergoing outpatient surgery and focuses on, although is not limited to, cardiac, pulmonary, and neurological systems, those most likely to be affected by ECT. The patient's past experience with anesthesia should be elicited, as well as family history of capacity to tolerate anesthesia. Most providers document a complete blood count and electrolytes as well as an electrocardiogram. In addition, a chest X-ray, liver function tests, a complete metabolic panel, and a pregnancy test for women of child-bearing age may be needed. A brief dental exam for loose or missing teeth and the presence of bridges and dentures is recommended. Testing of plasma pseudocholinesterase or dibucaine number is done as indicated by patient and family history. The risk of fracture of the long bones or spine has been averted by the use of muscle relaxants. Hence, spinal X-rays are done as indicated by a patient's history of skeletal injury or disease. Brain imaging is recommended when a questionable neurocognitive history, focal findings on neurological or fundoscopic exams, or altered neurocognitive status are present. The basic medical evaluation should reveal whether there might be a need for further specialty consultations, testing, or labs. Many institutions involve an internist routinely, especially when comorbid conditions that can be affected by or interact with ECT (e.g., diabetes) will need management during the course of treatment.

Taken as a whole, the pretreatment evaluation will result in recommendations for the modification of medications the patient may be receiving, on both a medical and a psychiatric basis; the modification of ECT technique; the modification of anesthesia technique; and the management of both psychiatric and medical conditions during the ECT course.

Consent

Written informed consent is standard in the practice of ECT and involves a discussion of the risks and benefits of the treatment with the patient and/or legally sanctioned surrogate. Procedures for consent are locally regulated, particularly at the state level, and familiarity with these regulations is essential. Consent can include both the anesthetic procedures and the electrical stimulation, although institutions may provide separate consents for each of these aspects of treatment. Consent forms generally cover several different areas and resemble the type of document used for comparable medical or surgical procedures. Descriptions of the procedure and expected benefits are detailed. Risks of the treatment, including possible medical and cognitive adverse effects, including death, should be documented. The possibility of relapse and nonresponse should be addressed. Expected participation by or behavioral restrictions of the patient—e.g., taking nothing by mouth for several hours before treatment—should be spelled out. Alternatives to treatment, including no treatment, should be discussed. In addition to a generic description, patients should understand the individual indications and rationale for ECT. They should know who can answer any questions about the treatment that may occur during the course of ECT. It should also be clear that consent can be withdrawn during the course of treatment. The amount of information given should be tailored to each patient, recognizing that too much information can obscure the process just as too little can. Guidelines and sample consent documents are available from professional organizations.

Most patients referred for ECT have the capacity to consent and can give it [illegible]. Generally, capacity is assumed to be present unless there is strong evidence to the contrary. Where doubt exists as to capacity, an independent [illegible] may be prudent. It is important to weigh the protection of autonomy and the opportunity to receive effective treatment in the consent process. Although patients with capacity should not be coerced to receive treatment, [illegible] all patients who lack capacity should not be unnecessarily obstructed [illegible] receiving it, especially when ECT is being recommended to prevent severe adverse outcomes such as increased morbidity or even death. Although [illegible] vary by jurisdiction, most allow for involuntary treatment with surrogate consent and/or legal review, which can include formal judicial review. Some jurisdictions mandate not only judicial review, but also review by the [illegible] of health for patients who lack capacity and object to ECT.

Surrogates must proceed through the consent process in a similar way [illegible] with capacity. Family members and other significant associates [illegible] conversations are encouraged to become educated about ECT. Audiovisual [illegible] written material may be provided to patients, family, and others as [illegible]. Finally, it should be remembered that consent is a process throughout [illegible] course of ECT, and clinicians should maintain an open exchange about [illegible] response, side effects, and prognosis. Separate consent should be [illegible] for continuation or maintenance ECT because the indication changes [illegible] treatment to relapse or recurrence prevention, and the risk–benefit [illegible] may have changed as well.

Electrode Placement, Stimulus Waveform, and Dosing

Controlled trials in ECT over the last two decades have involved [illegible] the effect of varying aspects of ECT technique, most frequently electrode placement and stimulus dosing strategies, on response rates and adverse cognitive effects. Research from a prior era led to a belief that seizure elicitation was necessary and sufficient for efficacy because subconvulsive stimuli were associated with lower response rates in several studies. When attenuation of electrically induced seizures with lidocaine was also associated with reduced efficacy, adequate seizure duration was also postulated to be necessary for therapeutic response. These tenets have been revised in light of observations from modern studies, and current practice has been [illegible] greatly affected.

A series of studies since the 1980s has demonstrated that, dependent on the combination of electrode placement and stimulus dose, [illegible] could vary in eliciting clinical response from 20 to 70 percent. Recent studies using an ultrabrief-pulse stimulus configured the waveform in a more physiological way to minimize excess electrical dose, [illegible] to the substitution of brief-pulse waveforms for the original [illegible] waveforms. Right unilateral electrode placements were particularly affected by dose, and a dose–response relationship exists up to a [illegible] intensity of 8 to 12 times the seizure threshold. At an electrical dose [illegible] times the seizure threshold, right unilateral ECT is equivalent to bilateral ECT in clinical efficacy, but it maintains an advantage [illegible] producing fewer adverse cognitive effects. For an electrical dose [illegible] six times the threshold, the advantage in acute cognitive effects [illegible] be eroded, but there is evidence that an advantage in long-term [illegible] effects remains. These findings make dose relations with [illegible] threshold particularly critical for right unilateral ECT. Ultra- [illegible] right unilateral ECT at six times the seizure threshold is equally [illegible] to both brief-pulse bilateral ECT and brief-pulse right unilateral ECT. Ultrabrief bilateral ECT at 2.5 times the seizure threshold [illegible] ineffective treatment. Manipulation of waveform in this manner [illegible] even more powerful effects on cognitive outcomes than had [illegible] placement, with results for ultrabrief right unilateral ECT [illegible] practically indistinguishable from those obtained in cognitive test- [illegible] gender-, and intelligence quotient–matched medically and psychiatrically healthy controls. Combined with results of neurophysiologic and brain imaging studies of the effects of ECT, the clinical effect of the interaction of electrode placement and dose also suggests that the antidepressant effects of ECT depend on the anatomic specificity of the effects of current density rather than on seizure elicitation alone. It was also found that the speed of clinical response was enhanced as stimulus intensity was increased above the seizure threshold for both unilateral and bilateral electrode placements.

Although there has long been a theoretical interest in greater localization of the effects produced by electroconvulsive stimulation in brain tissue, the neurophysiological and clinical findings related to the interaction of electrode placement and stimulus intensity have rekindled interest in concentrating current density in prefrontal areas by manipulating electrode placement.

Electrode Placement. Historically, most practitioners have used bifrontotemporal electrode placement because of its reliability in producing efficacy and its ease of use. This electrode placement is also associated with more short- and long-term adverse cognitive effects and is more likely to produce delirium, which may require interrupting a course of ECT and perhaps even terminating it before optimal therapeutic effects have been obtained. Hence, when bifrontotemporal ECT is used, attention should be paid to restricting the dose to a moderately suprathreshold level to attenuate adverse cognitive effects as much as possible. It should be emphasized that the combination of ultrabrief pulse and bifrontotemporal electrode placement has not been demonstrated to be effective. Treatment with bilateral electrode placements, particularly a bifrontal configuration, is more likely to manifest EEG seizure without motor seizure, and EEG monitoring can be particularly useful in detecting its occurrence.

Newer electrode placements include bifrontal configuration and asymmetrical placements. There are limitations to these strategies, imposed by the fact that the high impedance of the skull and scalp causes spreading of the electrical stimulus and restricts possibilities for localization of the stimulus. Bifrontal electrode placement, with positioning far enough laterally to minimize interference with impedance relations, has been investigated, and there have been several demonstrations that bifrontal electrode placements are equally effective to bifrontotemporal and adequately dosed right unilateral electrode configurations. Evidence of advantages in sparing of cognitive effects is quite preliminary, and adequately powered investigations with more extensive and sensitive cognitive batteries are needed. Seizure threshold is likely to be relatively higher with bifrontal ECT.

The relatively better cognitive side effect profile of right unilateral ECT should encourage wider use now that the efficacy of this electrode placement can be assured with adequate dosing strategies. In contrast to bilateral ECT, a dose closer to 500 percent above the seizure threshold is more likely to assure efficacy. ECT devices in the United States are restricted to an output in the range of 504 to 576 mC. Approximately 90 percent of patients have seizure thresholds that can accommodate optimal dosing with brief-pulse right unilateral ECT, and the combination of right unilateral electrode placement with ultrabrief pulse width extends the range of U.S. devices so that most patients can be treated within these constraints. Individuals with exceptionally high seizure threshold may require bilateral electrode placements to remain within the device restrictions. Maximizing interelectrode distance by using the d'Elia placement may also be optimal. Many other right unilateral placements have been described, but there is little work to support their use (Fig. 31.34a–1).

There has been some concern that left-handed patients may require different electrode placement than right-handed patients, especially if unilateral placement is desired. Even when handedness is lateralized

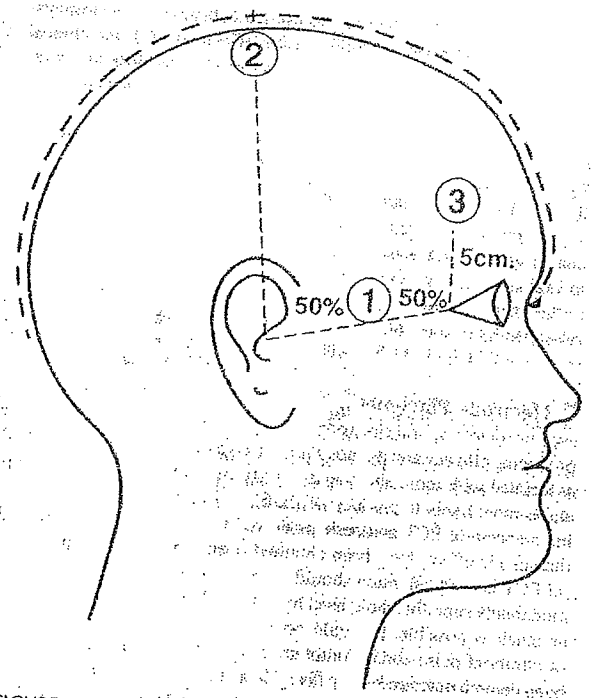

FIGURE 31.34a–1. Electrode placements. Position #1 represents the frontotemporal position, used for both electrodes, one on each side of the head, in conducting traditional bilateral ECT. For right unilateral ECT, one electrode will be in the right frontotemporal position, and the other will be just to the right of the vertex at position #2. Position #3 represents the frontal placement, used for both electrodes in conducting bifrontal ECT.

to the left, the anatomic localization of language function in 70 percent of left-handed individuals is the same as in those who are right-handed. Furthermore, there is evidence for independent lateralization of affect, with the right hemisphere involved in sustaining depressed mood regardless of handedness. Because of limited indications that affective function and efficacy of ECT are associated with handedness, handedness is not generally used to guide the choice of electrode placement.

Stimulus Waveform. The original ECT devices (1938 and for many years after) generated the electrical stimulus as a sine wave with a rather wide pulse, approximately 8.33 ms (60 Hz). Modification of the waveform to a bipolar rectangular pulse, 0.5 to 2.0 ms wide, represented an advance—diminishing nonessential electrical dose, dramatically reducing adverse cognitive effects, but preserving efficacy. Modern ECT devices retain this capability. However, neurophysiological observations suggest that the optimal pulse width for neuronal depolarization is actually in the range of 0.1 to 0.2 ms. Thus, a brief pulse width is inefficient and delivers unnecessary stimulation. Although reductions of pulse width to this extent may not be practical with current engineering of ECT devices, several reports, including randomized, controlled trial evidence, using a pulse width of 0.3 ms (known as "ultrabrief" in contrast to "brief") have demonstrated that right unilateral ECT, typically at six times the seizure threshold, is equivalent in efficacy to both right unilateral and bilateral ECT using brief pulse widths.

In one report, patients treated with the ultrabrief pulse showed significantly less impairment in acute, subacute, and long-term cognitive side effects of anterograde and retrograde memory than patients receiving standard pulse width stimulation for both unilateral and bifrontotemporal ECT. In fact, those who received ultrabrief right unilateral ECT did not deteriorate in any cognitive measure relative to pre-ECT performance. A second report comparing ultrabrief right unilateral and ultrabrief bifrontal ECT at 2.5 times the seizure threshold found no change or improvement in cognitive performance. A retrospective report investigating the outcomes of ultrabrief- and brief-pulse right unilateral ECT confirmed similar efficacy of the two pulse widths and advantages for ultrabrief pulse widths in cognitive performance.

Seizure Threshold and Dosing. The degree to which the electrical stimulus exceeds the seizure threshold, affects the efficacy of right unilateral ECT, the speed of clinical response regardless of electrode placement, and the cognitive side effects produced. These effects are in the same direction for each of these domains. The higher the stimulus dose, the better is the efficacy of right unilateral ECT (up to 8 to 12 times the seizure threshold); the quicker is the clinical response (by one or two treatments over a course), and the greater are the cognitive side effects. These observations have led to the promulgation of dosing methods to refine the stimulus intensity.

Strategies for determining stimulus dose include dosing based on empirical determination of seizure threshold (titration), formula-based dosing, and fixed dosing. Empirical titration involves an approximation of the seizure threshold in the first treatment session, followed by a calculation of optimal dose based on the results obtained. The stimulus intensity estimated on this basis is then generally used for the remaining sessions. The first electrical stimulus in the titration is set low enough that a seizure results in only a minority of patients. Restimulations at intervals of 20 to 60 seconds are given in the same session, using progressively greater amounts of charge until a seizure is produced.

The dose at which a seizure is elicited is termed the seizure threshold and has been found to vary at least 50-fold in patients undergoing ECT. Because of this wide variation in seizure threshold, dosing based on empirical titration is thought to be the most precise method of stimulus determination. Furthermore, it is safe for most patients when conducted with adequate physiological monitoring and the use of anticholinergic agents as appropriate to prevent the brief periods of bradycardia that may accompany subconvulsive stimulation. In controlled trials in which dosing was based on empirical titration, patients benefited clinically beginning with the first treatment session, even though the dose was given near threshold, a particular concern with right unilateral electrode placement. Seizure threshold, as empirically determined, increases over the course of ECT but returns to levels observed in the first treatment session within 1 week of ending treatment. Other measures of convulsant activity, such as seizure duration, may take up to 60 days to return to values observed in the first treatment session.

Formula-based dosing uses factors known to influence seizure threshold, such as age, electrode placement, stimulus pulse width, gender, and concomitant medications, including anesthetics, to estimate adequate stimulus intensity. Seizure threshold is generally higher in men than women, with bilateral electrode placement than with unilateral electrode placement, and with increasing age. It is unresolved whether bifrontal electrode placement results in differences in seizure threshold when compared with bifrontotemporal placement. The basis for these observations has not been extensively investigated. The simplest formulas use age alone, but even the most detailed and elaborate

formula can only account for about 40 percent of the variance in seizure threshold observed in patients. Hence, there has been limited success obtaining precision in seizure threshold approximation and dosing using formulas.

Fixed dosing occurs when the same dose of electrical stimulus is applied in all patients receiving ECT. It is obviously the easiest technically and maximizes the chances of clinical response, especially for right unilateral electrode placement. Unfortunately, this dosing strategy can cause patients with the lowest seizure thresholds to receive up to 20 times an adequate electrical stimulus, especially with bilateral electrode placement. For low-threshold patients, fixed dosing enhances the possibility of increased adverse cognitive side effects as a result. If fixed dosing is used with right unilateral electrode placement, the expected benefit in adverse cognitive effects could be lost. It is felt that *fixed dosing* may only be appropriate for patients with such serious medical conditions that even one subconvulsive stimulus, as is still a possibility with formula-based dosing, must be avoided.

Seizure threshold and subsequent dose determination can also be influenced by which stimulus parameters are adjusted. Comparisons of adjusting frequency versus stimulus train duration on brief pulse devices have indicated that longer duration is more efficient in eliciting seizures than increased frequency, although the effect sizes are small. Efficiency in seizure elicitation can also be optimized by using narrower pulse widths in setting the parameters on brief-pulse devices. This strategy has the additional effect of extending the range of devices that are capped in stimulus output. There also has been recent interest in optimizing pulse amplitude, with initial indications that further efficiencies may be obtained.

Anesthesia and Treatment Procedures. Because ECT is given under brief general anesthesia, the treatment is usually performed in a specific treatment area that generally meets standards for the performance of day surgery, including the capacity to manage medical emergencies and to recover patients postictally. The staffing commonly consists of a psychiatrist privileged to administer ECT, an anesthetist, and one or more nursing personnel. Although the anesthetist maintains responsibility for anesthesia procedures, particularly airway management, the treatment procedures are conducted collaboratively.

Before anesthesia is induced, appropriate physiological monitoring is instituted and continued until the patient is adequately recovered. Cardiac monitoring and pulse oximetry are standard; monitoring end-tidal carbon dioxide is also standard at many institutions. Automated noninvasive blood pressure monitoring, set at a short frequency, is common. Monitoring of seizure activity can involve observing both motor and electroencephalographic (EEG) seizure duration. Motor seizure duration can be determined optimally using the cuff method. A blood pressure cuff is applied to the forearm or just above the ankle and inflated to a level above the anticipated maximum systolic pressure (greater than 250 mm Hg) to prevent anesthetics from affecting muscle contraction in the distal limb. Motor movements resulting from seizure induction can then be directly observed. The cuff should be ipsilateral to electrode placement for unilateral ECT. Ictal movements may continue longer in the face and neck. Use of the cuff method may not be appropriate for patients with severe peripheral vascular conditions, especially in the lower limbs. Many ECT devices have incorporated technology to allow at least two-lead EEG monitoring, with a frontal-mastoid montage preferred. Care must be taken to prepare EEG sites adequately and to take into account artifacts, such as ECG and movement.

Oxygenation is provided using 100 percent O_2 via mask and administered under positive pressure when respirations have stopped secondary to anesthesia medications. Respiratory support is discontinued when there is return of spontaneous respiration adequate to maintain clinically acceptable hemoglobin saturation on room air. Preoxygenation may begin even earlier in the sequence of treatment procedures when medical conditions such as obesity or pulmonary disease pose a risk to respiratory function. In rare circumstances, such as third trimester pregnancy, patients may be intubated.

There is variation in the use of anesthetic medications. Not all practitioners employ anticholinergic medications pre-ECT, and, unfortunately, controlled studies comparing ECT with and without these agents did not include those patients at greatest risk for cardiovascular conditions. Anticholinergic medications such as atropine and glycopyrrolate are used to dry secretions that might interfere with respiration under anesthesia and to decrease the vagally mediated bradycardia and even asystole that may occur immediately after the electrical stimulus is administered. The cardiac effects of anticholinergic agents are most useful in the following clinical situations: During seizure threshold titration, when subconvulsive stimuli will not be accompanied by compensatory catecholaminergic output; in the presence of agents that promote bradycardia, for example, β-blockers; and when cardiac conditions characterized by some degree of electrical blockade are preexistent. Anticholinergic agents may be contraindicated when they might provoke preexisting arrhythmias or threaten cardiac compensation through increases in workload from higher heart rate. Although glycopyrrolate does not cross the blood–brain barrier under normal circumstances and could have an advantage over atropine, controlled comparisons with atropine have not detected differences in cognitive adverse effects or postictal nausea.

Ultrabrief general anesthetics are used to induce unconsciousness while muscle relaxants are in effect and during seizure elicitation. Methohexital, a short-acting barbiturate, has been the preferred agent in the United States. Alternative anesthetics include another short-acting barbiturate, thiopental, and short-acting agents from a variety of classes, including propofol, etomidate, and ketamine. Thiopental has been associated with a higher incidence of postictal arrhythmias compared to methohexital, and its pharmacological properties can be associated with long recovery periods when higher doses are used. Propofol reduces hemodynamic changes accompanying ECT and typically produces a rapid, smooth recovery. Its antiemetic properties can be useful when patients develop nausea or vomiting. This agent also attenuates seizure duration, but studies comparing it to more standard agents have not detected differences in clinical efficacy or cognitive recovery. Agents that attenuate seizure duration generally are associated with slightly shorter emergence and recovery, although a recent review concluded that the differences, while statistically significant, were not of sufficient magnitude to affect the choice of agent. Numerous reports have explored the addition of short-acting opioids, such as remifentanil, to standard agents. In general, less of the standard agent is required, and seizure durations can be longer. Etomidate does not affect seizure threshold and is associated with fewer cardiac side effects, especially when compared to propofol. Etomidate can also produce myoclonus, and repeated use in animals has been associated with reductions in adrenal function. Ketamine has been associated with longer seizures in animals given ECS and has been hypothesized to be independently an antidepressant and possibly neuroprotective, with shorter recovery time and better anterograde memory functioning observed in some reports. Unfortunately, its sympathomimetic properties can result in hallucination and unusual states of consciousness, as well as increases in heart rate and blood pressure. Insufficient study has been conducted to make certain conclusions regarding its use in ECT. Until recently, both etomidate and ketamine have been reserved for situations in which seizure elicitation is difficult. Greater attention to adequate dosing of these anesthetic agents has become increasingly important as the increased use of cognitively sparing techniques, such as ultrabrief right unilateral ECT, have been accompanied by reports of patients regaining awareness and remembering the effects of succinylcholine before full respiratory capacity returns to baseline.

Before the development of muscle relaxants, musculoskeletal injury, particularly fracture of the long bones or vertebrae, was not uncommon, as it is today. Curare was developed to reduce the tonic–clonic movements produced by electrical induction of a generalized seizure, but its use has been superseded by that of succinylcholine, a depolarizing agent with rapid onset and brief duration. Myalgia can be a side effect of succinylcholine. This usually minor muscle pain can be reduced by using curare before administering succinylcholine, although patients may find the experience of weakness induced by curare unpleasant. An alternative to curare in treating these myalgias

which are often present in only the first few treatments, is the use of common analgesics. Although modification of movement is the usual goal of using muscle relaxants, complete paralysis may be desirable when there is a history of skeletal disease, such as osteoporosis or recent fracture. When the use of succinylcholine is contraindicated, as in pseudocholinesterase deficiency, nondepolarizing agents can be used. Agents available in the U.S. market are rather longer acting; even when reversal is produced with an anticholinesterase such as neostigmine, it may be at least 1 hour before recovery is sufficient for transfer from the ECT treatment area to a recovery area to be safe.

Although complications of ECT have involved the cardiovascular system most commonly, there is controversy regarding the routine use of agents, such as β-blockers, that reduce the increases in hemodynamic activity that accompany ECT. Controlled studies of routine use do not demonstrate advantages for active intervention, perhaps because the patients who benefit are a minority of the entire population of ECT recipients, most of whom easily tolerate the observed increases in heart rate and blood pressure for a few minutes. There has also been some concern that the hypermetabolic cerebral state induced by the treatment requires a corresponding increase in cardiovascular functional level to maintain adequate oxygenation and nutrient supply to the central nervous system. The conservative position is to restrict the use of pharmacological intervention to those conditions in which the need is unambiguous, such as aneurysm, sustained hypertension, and/or tachycardia.

Because the application of the electrical stimulus directly stimulates contraction of the jaw muscles, a bite block is placed in the mouth just before the delivery of the electrical stimulus to protect the teeth and oral soft tissues. The duration of the stimulus can be several seconds but typically is only a few. The duration of the seizure is commonly less than 1 minute. The relationship of duration to efficacy has been questioned because of recent findings, and it is clear that duration alone is insufficient to ensure clinical adequacy. Seizures of less than 15 seconds can occur close to the seizure threshold and are often considered abortive. Seizures of similar duration can also be observed in the elderly, late in a treatment course, and with markedly suprathreshold dose, but such short-duration seizures may not be associated with lack of adequacy. These circumstances highlight the usefulness of empirical titration techniques to inform the practitioner more exactly about seizure threshold and dose and to guide what actions, if any, to take when short seizures occur. Seizures longer than 3 minutes, with either motor or EEG monitoring, are considered prolonged and should be actively controlled using intravenous anticonvulsants, such as the short-acting barbiturate used to induce anesthesia or benzodiazepines. The occurrence of long-duration seizures is unusual, except in the youngest patients, and the cause of such long duration should be investigated, especially if it was not easily terminated.

Patients are recovered with monitoring of cardiovascular and respiratory functioning until physiologically stable. If the patient is not awake and oriented at that time, further recovery is needed until the patient is alert and reoriented. Many facilities require that the patient be fully ambulatory before leaving the treatment and recovery areas. Bed rest may be needed for a period of time. Side effects, such as headache and nausea, are monitored and treated as needed. Headache frequently responds to analgesics, especially cyclooxygenase inhibitors; patients with migraine may require more specific antimigraine treatments. Postictal delirium with agitation, disorientation, and lack of full consciousness occurs in a minority of patients. Decreasing environmental stimulation and securing protection may be adequate management, but, not infrequently, patients require intravenous pharmacological intervention with sedatives and prophylaxis at subsequent treatments.

Treatment Course. Typically, ECT is given [illegible] times weekly on nonconsecutive days. The latter frequency is common in the United States. Twice-weekly treatment is [illegible] compared with thrice-weekly treatment, takes longer to [illegible] and is associated with fewer acute cognitive side effects. [illegible] quencies of treatment are more problematic. Daily treatment is [illegible] done now, but at one time it was believed to speed [illegible] cally and was used in the most urgent situations, such as [illegible] This treatment schedule was also characterized by a risk of [illegible] severe cognitive side effects, especially when a course [illegible] gressive ECT was used. In addition to being logistically difficult to obtain in many places, the risks appear to outweigh the benefits, and daily treatment is no longer advised. Another approach to increasing frequency was to elicit more than one generalized seizure per session under continuous anesthesia, known as multiple monitored ECT (MMECT). Similar to daily ECT, the goal was to accelerate clinical response with the additional advantage of decreasing the number of times anesthesia is delivered. Although there have been both reports of uncontrolled observations and one controlled trial concerning MMECT, the literature is clear that severe adverse events accompany this treatment approach with only modest gains in efficiency of response. Of most concern are reports of cardiovascular morbidity and mortality, as well as serious adverse cognitive effects, including prolonged confusion. Although there may be a place for the use of MMECT, it is used only in extremely unusual circumstances, such as intractable seizures, and should be restricted to double stimulus sessions. At the other end of frequency, once-weekly ECT is associated with a weaker clinical response and is more suitable for continuation ECT schedules as opposed to acute treatment.

The number of treatment sessions in a course of ECT should be individualized because patients vary in this requirement from [illegible] sessions to more than 15, especially when changes in treatment technique have been made. The course length cannot be predicted, although the average is from 6 to 12 sessions. Fixed course lengths are not appropriate for these reasons. Patients should be evaluated after one to two treatments for clinical response and adverse side effects, particularly cognitive effects. These assessments are best done between treatment days when the acute effects of anesthesia and ECT will interfere less with evaluation. Treatment should end when there is remission of target symptoms or when further improvement has not occurred over two or three sessions with optimal technique.

When response is inadequate, modifications can be considered. Such modifications can include intensification of stimulus energy by increasing the charge through manipulations of the various parameters of the stimulus or by changing electrode placements. Since threshold increases over the course of treatment, so higher stimulus intensity may be useful later in a treatment course if responses inadequate. If any medications with anticonvulsant properties, including barbiturate anesthetics or propofol, are being used, discontinuation or decreasing dose should be evaluated, particularly when the patient has a high seizure threshold. At least 10 treatments with optimal electrode placement and dosing should be given before nonresponse is declared. When course length exceeds 15 to 20 sessions, especially with modifications of technique, reconsideration of the use of ECT with careful balancing of the risk of an unresolved episode of illness against the risk of accumulating adverse effects, should be undertaken. Additional consultation, with reassessment of primary and comorbid diagnoses, may be advisable.

ECT is the only treatment for major psychiatric syndromes that is discontinued when remission occurs. Hence it is not surprising that a significant proportion of patients who relapse do so within the

first few weeks of termination of ECT and may require further ECT. Often additional ECT is given along with medications that will be used for continuation and maintenance of remission. Although not yet examined in a controlled trial, tapering the termination of ECT by decreasing frequency of sessions while medications are stabilized and produce their effects may be a more effective strategy for relapse prevention.

Continuation Treatment. Continuation treatment, that is, treatment for 6 months beyond remission of an acute episode of illness to prevent relapse, is standard practice for the major syndromes that are somatically treated. It is recommended and routine post-ECT as well. Populations that receive ECT are particularly likely to be characterized by risk factors for relapse: Medication resistance and the presence of psychotic features. At least half and upward of 85 percent of ECT responders in some samples will relapse without continuation treatment particularly in the first several weeks posttreatment. Aggressive continuation treatment should be initiated as soon as remission is evident, although initiation of pharmacology during the ECT course itself has not been shown to be of additional benefit.

Continuation treatment with medications is the predominant practice post-ECT. This has been based on studies conducted in the 1960s in Great Britain and on clinical experience. The class of agent advised matched that used in the absence of ECT: Antidepressants for unipolar depression, antidepressants and mood stabilizers for bipolar depression, mood stabilizers with or without antipsychotics for mania, and antipsychotics for schizophrenia. Studies in the 1970s found little support for the use of lithium alone as relapse prevention following depression but there is some support for lithium as maintenance treatment after 6 months of remission to prevent recurrence once remission is firmly established. The first randomized, prospective, controlled study of continuation treatment post-ECT in unipolar patients confirmed substantial relapse rates on placebo (84 percent) but only moderate improvement in relapse rate on the antidepressant nortriptyline alone (60 percent). The relapse rate in unipolar depression was significantly reduced in this study by the addition of lithium to nortriptyline (39 percent), with most of the relapse in this arm of the study occurring in the first 5 weeks. Randomization had been stratified by medication resistance and (mood congruent) psychosis, but psychotic patients did not relapse more frequently. Medication dose was in the range used for acute treatment. A prospective trial of combination antidepressant and antipsychotic continuation treatment post-ECT did not find an advantage for combination treatment over antidepressant alone in an elderly population, and the combination treatment was found to be associated with greater frequency of side effects. A recent randomized, controlled trial found no advantage for beginning nortriptyline or venlafaxine during the course of ECT in preventing relapse. Observations of community practice post-ECT yield relapse rates similar to those found in the randomized, controlled trial assignments using antidepressants alone. Little is known about the use of second- and third-generation agents or anticonvulsant mood stabilizers in relapse prevention. There are preliminary studies suggesting that relapse prevention is more effective when using a class of antidepressant that was not found to be ineffective prior to ECT treatment. Modern practice suggests sparing use of antidepressants in bipolar patients. Little work in pharmacological relapse prevention post-ECT for any other diagnosis than depression has been done in the modern era.

ECT was introduced before the psychopharmacological era; thus, administering ECT after an index episode was not uncommon early in the history of ECT use. With ECT populations becoming increasingly medication resistant and various pharmacological strategies still characterized by relapse rates in the range of 40 percent, there is renewed interest in continuation ECT for patients who relapse on continuation pharmacology. The first randomized, controlled comparison of continuation ECT in a fixed schedule with the combination of nortriptyline and lithium did not show an advantage for ECT and confirmed relapse rates observed in prior studies; relapse escalated when the schedule of administration dropped below once weekly. Other prospective data confirmed these observations. Recent prospective, controlled, nonrandomized data, as well as post hoc analyses from the randomized, controlled trial, support the practice of tapering ECT after an acute course, combining ECT and pharmacology as continuation treatments, and using a symptom-driven, flexible schedule of ECT administration to improve relapse prevention.

Recommendations from professional organizations have guided various aspects of the practice of continuation ECT, although these bodies use differing thresholds for evidence when recommending strategies, a circumstance most notable when the National Institute for Health and Clinical Excellence in the United Kingdom issued guidelines in conflict with the Royal College of Psychiatrists, as well as other with professional bodies in the Commonwealth and globally. Suitable patients should have recurrent illness, demonstrated response to ECT, intolerance of or relapse on continuation medications, and ability to comply with continuation ECT protocols, particularly behavioral prescriptions, such as fasting prior to the procedure, and restrictions, such as refraining from important decision making for a period of time following each treatment. Generally, continuation ECT uses the electrode placement and dose that produced remission. A taper of ECT from the acute phase to the continuation phase has become common. Treatment frequency is gradually extended between treatment sessions, as tolerated, to monthly or even less often. It is thought that if patients remain well 2 months or more, they are out of episode, and the discontinuation of continuation treatment can be entertained. Continuation ECT is almost always given in an outpatient setting. Cognitive functioning should be monitored, as well as the status of psychiatric symptoms and medical fitness for each session. There has been one promising but uncontrolled pilot study of the use of cognitive behavioral therapy to augment somatic continuation treatments post-ECT.

Maintenance treatments are those given beyond the 6-month continuation treatment period, and the purpose of these treatments is prevention of recurrence. Because patients receiving ECT in current practice are almost always suffering from highly recurrent illness, maintenance treatment can be entertained for most ECT responders who do not relapse with continuation treatments. There are now several controlled observations of the use of maintenance ECT up to 4 years with positive outcomes in relapse prevention for depression. Japanese investigators published recent case series on the use of ECT as a maintenance strategy for treatment-resistant schizophreniform and catatonic illness. Individual decisions about maintenance treatment should be informed by the number, frequency, and intensity of prior episodes; the ability to tolerate continued treatment; the ability to comply with treatment; the experience when attempts to taper treatment are made; and patient preference. Again the standard will be maintenance medications. Maintenance ECT is also available, especially for those patients undergoing continuation ECT when medications have proved inadequate. Maintenance ECT is similar in many aspects to continuation ECT, and it is performed at the longest intervals to sustain remission. There is no evidence that there is a lifetime maximum number of ECT courses.

INTERACTIONS OF MEDICATIONS AND ECT

ECT can interact with medications given for psychiatric, as well as medical, conditions. As such, it may be necessary to make changes in a patient's drug regimen when a course of ECT is undertaken. These changes can include tapering, withdrawing, augmenting, or adjusting the timing of administration of medications. Some psychotropics and

many drugs for medical indications are continued. Medications that are already a part of the patient's treatment regimen and are expected to mitigate physiological changes that accompany ECT or protect against adverse reactions to ECT or anesthesia are often given the morning of treatment. Examples are antihypertensives, inhalers for pulmonary conditions, and steroids, although anesthetists may wish to substitute intravenous steroids for oral steroids pre-ECT. It appears that stress doses of steroids may not be necessary at ECT. The administration of β-blockers pre-ECT should be carefully evaluated because of the propensity of this class of agents to enhance bradycardia or precipitate asystole; use of atropine pre-ECT should be considered in this circumstance. Labetalol crosses the blood–brain barrier and attenuates regional CBF at ECT; both esmolol and labetalol are anticonvulsant at doses used in this setting. Lidocaine and its analogs can interfere with seizure induction and should be withheld. Other medications that should be held until after recovery are diuretics, hypoglycemics, including insulin, depending on an individual evaluation of the patient's needs, and long-acting cholinesterase inhibitors for glaucoma that may interfere with anesthesia recovery.

Medications that can result in severe adverse reactions include theophylline and lithium. Theophylline is a member of a class of agents that are known to increase seizure duration, and theophylline can result in status epilepticus, even at therapeutic levels, when administered during an ECT course. In fact, caffeine, a short-acting member of the same class of medications as theophylline, had been used to increase seizure duration when seizure length was thought to be a critical parameter to ECT efficacy. Inhaled bronchodilators and steroids, as well as other oral and inhaled agents, have replaced theophylline in modern pulmonary practice to a great extent. If theophylline is part of the therapeutic regimen and ECT is undertaken, consultation to evaluate the possibility of a substitute regimen is generally sought. Lithium combined with ECT has been shown to result in confusional states, serotonin syndrome, and prolonged and/or focal seizures. Although it is not neurotoxic in all patients and the toxicity of the combination may be dose related, discontinuation of lithium is frequently undertaken in an acute course of ECT. For continuation and maintenance ECT, doses are often withheld for 24 hours prior to treatment, allowing for washout and markedly diminishing the chance of negative interaction. Another class of medications that can pose increased risk are β-lactam antibiotics and ciprofloxin, which are proconvulsant and have been associated with seizures in non-ECT patients and tardive seizures during a course of ECT.

Anticonvulsants can increase seizure threshold and decrease seizure expression, and they might interfere with the efficacy of ECT. When used for control of a seizure disorder, they are continued without alteration unless poor seizure expression occurs along with weak response. In this circumstance, levels of drug may be reevaluated in consultation with neurology. If anticonvulsants are used for psychiatric indications, they are generally discontinued to prevent a negative effect on clinical response.

Benzodiazepines are also anticonvulsant, but they are more often used for psychiatric indications. There are reports of diminished efficacy when benzodiazepines are used in conjunction with ECT, especially right unilateral electrode placement. As a result, this class of medications is tapered to the least necessary dose or discontinued. If the use of benzodiazepines is considered necessary for the management of severe behavioral syndromes, agents with shorter half-lives are preferable and should be withheld several hours prior to treatment. The use of flumazenil to reverse benzodiazepines has been reported but requires further study, and benzodiazepines may need to be administered during recovery to abort possible withdrawal. Little is known about the interaction of other sedative/hypnotics with ECT.

Anesthetists have been averse to allowing the use of monoamine oxidase inhibitors (MAOIs) concurrently with electroconvulsive therapy due to a potential for interference with management of cardiovascular abnormalities that may arise at treatment. ECT seldom results in a situation in which the use of vasopressors, which would not be mobilized because of interference by the recent use of MAOIs, is necessary. Hence, the literature includes many reports of the safe performance of ECT in the presence of MAOIs. Current practice allows for consultation between the psychiatric and anesthetic practitioners as to the best recommendation for any particular individual or practice setting.

An augmenting effect for neuroleptics when combined with ECT in schizophrenia can be accepted with some confidence. As discussed previously, the combination treatment is more effective than ECT alone and may be more effective than medications alone. A few studies even suggested that the long-term outcome of schizophrenia may be enhanced by combination treatment. Whether the augmenting long-term effects carry over to other psychotic conditions is not clear; there is evidence that they play no augmenting role in nonpsychotic depression. Most of the published data involve the use of typical neuroleptics. It appears that low-potency typical antipsychotics may be proconvulsant; haloperidol and fluphenazine appear to have little effect on parameters of seizure quality. The use of ECT combined with atypical neuroleptics appears to be safe. Clozapine and olanzapine have been observed to have proconvulsant properties, and quetiapine has anticonvulsant properties. Because of these circumstances, dosages of neuroleptics should generally be in the moderate range. The only antipsychotic that cannot be combined safely with ECT is resperidone.

Earlier work with tricyclics (TCAs) and MAOIs provided some evidence to recommend the use of antidepressants to augment ECT. A recent randomized, controlled trial found that both nortriptyline and venlafaxine increased the response rate to ECT by about 15 percent; nortriptyline was associated with diminished cognitive effects, whereas venlafaxine was associated with increased adverse cognitive effects. The combination of ECT and antidepressants is common practice in many parts of the world. Increasingly, in the United States psychotropics, including antidepressants, are continued during a course of ECT because of expanding limitations placed by insurers on the use of mental health resources. It appears that TCAs are safe in noncardiac populations and selective serotonin reuptake inhibitors in most populations, although they can increase seizure duration. After publication of a series of cases in which asystole occurred at doses of venlafaxine greater than 225 mg with the concurrent use of atropine, it might be advisable to limit the dose of venlafaxine if it is combined with ECT. The well-known proconvulsant effect of bupropion prompts caution in combining it with ECT in the absence of data documenting a clear benefit in doing so. It is unknown whether newer medications now used more frequently for depression have augmenting effects.

Finally, there has been limited interest in pharmacological approaches to mitigating the cognitive side effects of ECT. Preliminary data using physostigmine, thyrotropin-releasing hormone, and nalone have been published, but whether clinically significant effects could be obtained remains in doubt.

PHYSIOLOGY, ADVERSE EFFECTS, AND CONTRAINDICATIONS TO ECT

ECT is generally low risk and one of the safest procedures performed under general anesthesia. The estimated risk of serious complications, occurring in about 1 in 1,000 patients, is similar to that of general anesthesia for minor medical procedures. Risk of death, likewise in the range of that observed for such procedures, is about 1 in

in 100 patients in modern populations undergoing ECT. It has been argued this rate is less than the spontaneous death rate in comparable community-dwelling populations. Some believe that these rates of serious complications and death are lower than those related to the use of antidepressant medications. The most recent documentation of these rates—the mandated reporting of deaths occurring during and up to 14 days post-ECT in Texas—revealed only one death related to the procedure in the first 5 years. Although cardiac complications are considered to be the most common cause of morbidity and mortality, this death was due to laryngospasm. Cardiac deaths in this population were unrelated to ECT.

Cardiovascular System

The ECT procedure routinely results in parasympathetic outflow during and immediately after the electrical stimulus. Unopposed by anticholinergic medications, sinus bradycardia and even brief, clinically insignificant asystole can occur as a result. In patients older than 50 years of age, supraventricular ectopic beats are common but clinically insignificant. In vulnerable patients, vagally related arrhythmias can occur, such as atrial, junctional, and nodal rhythms, as well as atrial flutter and atrial fibrillation. Following parasympathetic stimulation, sympathetic output increases, mainly during the electrical stimulation and specifically when the adrenal gland also releases catecholamines. As a consequence, heart rate, blood pressure, and, perhaps most important, rate pressure product increase. These increases peak immediately postictally and drop off within minutes to pre-ECT values, although in those older than 50 years of age normalization takes up to 1 hour for blood pressure and longer for heart rate. There can be a short period of decreased heart rate at about 5 minutes post-ECT. Related abnormalities of cardiac rhythm that can appear include bradycardia and bigeminy, which are generally benign. Repolarization abnormalities such as T wave changes and ST segment depression can appear infrequently. Ventricular tachycardia, usually nonsustained, and fibrillation can occur rarely. About 55 percent of those with preexisting cardiovascular abnormalities manifest some abnormality in the course of ECT.

With judicious pretreatment evaluation of both the risks and benefits of ECT, cardiac consultation, and the stabilization of any underlying cardiac disease, many of the more serious cardiac complications can be avoided. About 90 percent of these patients will be able to complete a course of ECT safely. For example, ECT has been administered to patients with pulmonary hypertension, acute myocardial infarction, abdominal aortic aneurysm, and Takatsubo's syndrome. In patients with myocardial infarct, a period of time must be allowed for healing, but the risk relates not only to the time elapsed, but also to the severity of resulting cardiac compromise. As with arrhythmias and congestive heart failure, stress testing can be informative in deciding whether a patient can undergo ECT. The presence of a pacemaker or device to abort arrhythmias is not a contraindication to ECT. ECT has been administered without complication to stable patients with transplanted hearts.

Respiratory System

Along with cardiac complications, adverse events related to pulmonary function are a leading cause of morbidity and mortality associated with ECT. Most of the effects are associated with anesthesia procedures rather than the physiology of ECT per se. The use of muscle relaxants leads to the cessation of breathing, and oxygen delivered by positive pressure through a mask substitutes. When patients have underlying pulmonary disease, exacerbation of asthma or chronic obstructive pulmonary disease is possible, as well as excess secretions and aspiration. Rare cases of negative-pressure pulmonary edema have been attributed to inspiration against an obstructed airway or mechanical factors precipitating laryngospasm; it can also be neurogenically induced by the onset of status epilepticus. With proper preparation pre-ECT and anesthetic technique, these events are uncommon. Obstructive sleep apnea, at risk or may even be discovered during ECT anesthesia; it can usually be managed acutely with pre-oxygenation and the use of nasal pharyngeal or laryngeal mask. Another rarely observed complication is apnea resulting from slow metabolism of succinylcholine due to pseudocholinesterase deficiency. Supportive therapy suffices to manage this complication, and subsequent sessions of ECT can be given with a nondepolarizing agent.

Central Nervous System

Seizure induction results in a hypermetabolic state characterized by increased blood flow with significant elevation in oxygen and glucose consumption. Increased blood–brain barrier permeability has been hypothesized due to capillary hypertension. Postictally, metabolic suppression develops. These physiological changes have not been demonstrated to produce structural brain changes or damage in well-designed and controlled animal and human studies or by brain imaging or analyses of cerebrospinal fluid. There is insufficient energy, even at maximal output of a modern brief-pulse device, to cause brain tissue injury by temperature elevation.

ECT can be complicated by prolonged seizure duration, defined as greater than 3 minutes by motor or EEG measurement, which occurs in 1 to 2 percent of treatment sessions. The risk is greater in adolescents and young adults. There is a risk of structural brain injury along with cardiovascular and pulmonary complications if the seizure persists beyond 30 minutes even when oxygenation is adequate. Termination is undertaken using either parenteral benzodiazepines or the short-acting barbiturate used for anesthesia. If this fails, a standard protocol for status epilepticus treatment may be instituted. Patients who experience prolonged seizures need to be reassessed for underlying etiology. Prolonged seizures are more common in the presence of proconvulsant medications such as theophylline or lithium and probably trazodone or when more than one seizure is induced in a single session. They are also associated with medical conditions that decrease seizure threshold, such as electrolyte abnormalities and epilepsy. Nonconvulsive status should be suspected if there is lack of recovery from anesthesia or abnormalities in mental status persist. This state may be detectable by EEG monitoring but can be present when the typical two-lead EEG does not exhibit abnormalities. Tardive seizures are rare. The rate of onset of new seizure disorder after ECT does not exceed baseline rates in the general population. ECT can be given safely to patients with epilepsy.

Before the development of brain imaging, deaths and neurological deterioration were reported when ECT was given to patients with occult brain tumors and brain metastases. Evaluation, including radiological procedures, of patients with neurological findings or abnormal mental status now most often leads to the identification and treatment of such diseases prior to any administration of ECT. It is possible for ECT to be given safely to patients with small, slow-growing tumors without associated increased intracranial pressure, such as meningiomas. ECT has also been given to patients with healed skull and brain trauma, including craniotomy, as long as any skull defect is avoided. Patients may also experience transient central nervous system (CNS) symptoms of almost any variety—for example, various cortical sensory abnormalities.

Depression not uncommonly complicates CNS disease such as stroke and dementia. If patients with stroke are neurologically stable several weeks after a cerebrovascular event, ECT may be given. Attention should be paid to the treatment and stabilization of the underlying cause of the stroke, as well as to the current neurological status. Patients with dementia receive ECT for complicating depression but are at risk for greater adverse cognitive effects, such as delirium or prolonged confusion. There is interest in using the treatment for agitation-complicating dementia but little supporting, controlled evidence. Treatment using techniques focused on mitigating cognitive effects, such as right unilateral electrode placement, specific tailoring of dose, brief pulse waveform, and twice-weekly frequency, are often used.

Dental

Due to direct stimulation of jaw muscles during delivery of the electrical stimulus, patients bite down, sometimes strongly, and unstable teeth may be broken or dislodged completely. Also vulnerable are front teeth with crowns or other dental modifications such as laminates. The approach to this complication is routine prophylactic screening, and may necessitate dental consultation and procedures prior to ECT. If teeth are injured during treatment, care must be taken to remove any broken fragments before respiration resumes, when they may obstruct the patient's airway.

Musculoskeletal

With the consistent use of muscle relaxants, the most serious of these adverse effects is only of historical interest. Before the development of curare and later succinylcholine, fracture of the long bones or spine occurred in up to 10 percent of patients as a consequence of unmodified movements associated with seizure induction and expression. The usual patient, who receives enough muscle relaxant to modify movement rather that fully abolish it, has no significant musculoskeletal complications. Those with skeletal disease, such as osteoporosis, are more fully paralyzed for treatment. Although this complication has been almost completely abolished, elderly patients remain at risk for falls during a course of ECT, and appropriate fall precaution protocols should be used.

More common in the modern era and, ironically, often an adverse effect of depolarizing agents, is myalgia. These muscle pains are a consequence of the fasciculations produced during depolarization and are most prominent after the first treatment but seldom present after a few more sessions. Although myalgia can be mitigated by the use of curare along with succinylcholine, it can also be managed symptomatically with analgesics with the advantage of not prolonging or complicating the treatment session.

Patients with temporomandibular joint problems may experience an exacerbation of pain resulting from the unmodified contraction of jaw muscles during stimulus delivery. Spasm can also be induced. Prophylactic approaches may be advisable, such as the use of dental appliances already in the patient's possession or the administration of prophylactic analgesics such as nonsteroidal antiinflammatory medications. Symptomatic post-ECT approaches may also suffice.

Neurocognitive

Cognitive side effects are a major limitation to the use of ECT, although in recent years the syndrome of postoperative cognitive dysfunction has been detected in patients undergoing medical procedures requiring either regional or general anesthesia, with up to 10 to 20 percent, particularly those older than 60 years, affected. With ECT, these effects have been best described for depressed populations. The phenomena are made more difficult to discriminate because depression itself is accompanied by impairments in attention, concentration, and learning. Post-ECT, with remission of depression, attention and concentration are improved. Several factors influence the likelihood and extent to which impairments develop, but response to treatment is not a variable in the development of these cognitive adverse effects. Furthermore, functions such as reasoning, creativity, and the ability to form memories are not affected in any enduring fashion. Nondeclarative memory, that is, procedural memory and priming, does not appear to be affected either. It is also important to note that objective measurement and subjective report of cognitive side effects do not correlate.

The first factor in the development of adverse cognitive side effects is the time point in treatment, which influences not only severity, but also the type of effect observed. Disorientation, diminished processing speed, decreased anterograde and retrograde memory, and errors in visual-spatial function and word finding are greatest immediately after a treatment session. These effects diminish fairly quickly once the treatment course ends. Except for retrograde memory impairment, other cognitive effects generally return to pre-ECT baseline or even improve over baseline with right unilateral ECT. Diminished processing speed persists when sine wave ECT has been administered. Retrograde memory improves more gradually, but spotty deficits may persist, with recent memories for public information more vulnerable than older memories for personal experiences. Retrograde memory deficits may persist several months after treatment ends. In a community setting, 12.4 percent of patients manifested marked and persistent retrograde amnesia, defined as deterioration in autobiographical memory of at least two standard deviations from pre-ECT baseline at 6 months post-ECT. The only significantly correlated technical factor was the number of bilateral ECT; female sex was the only demographic or clinical factor to reach significance.

The likelihood of developing adverse cognitive effects is influenced by technical factors in the treatment: Bilateral electrode placement; inefficient stimulus waveforms, including brief pulse, but most particularly sine waveform; markedly suprathreshold dosing; greater frequency and number of treatments; and larger doses of anesthesia are more likely to result in deficits in the acute and subacute courses of treatment. Bilateral electrode placement associated with greater likelihood of persistent retrograde memory deficits long-term. In recent decades, sine waveforms, which are no longer recommended, have been largely replaced by brief pulse and, most recently, ultrabrief stimulation, and much has been learned about optimizing right unilateral electrode placement and restricting dose while maintaining efficacy (Table 31.34a–3).

Table 31.34a–3. Treatment Factors Influencing the Degree of Adverse Cognitive Effects from Electroconvulsive Therapy

Treatment Factor	Technique Associated with Fewer Adverse Cognitive Effects
Electrode placement	Right unilateral
Stimulus waveform	Ultrabrief (and brief pulse)
Stimulus intensity	Threshold determination, dose to threshold
Number of treatments	Fewest necessary for therapeutic effect or plateau of target symptoms
Frequency of treatment sessions	Less frequent, e.g., three weekly for acute treatment
Number of seizures per session	One
Simultaneous use of psychotropic medications	Discontinue lithium, second dose of neuroleptics
Dose of anesthetic medications	Adjust dose to produce light anesthesia; ketamine

Patient characteristics and clinical factors also affect the frequency and severity of adverse cognitive effects. Those with baseline neurological disease, magnetic resonance imaging abnormalities, and baseline impairments in global cognitive functioning are more vulnerable to developing deficits, as are older and female patients. The concurrent use of certain medications, such as lithium or medications with anticholinergic effects also increases the risk of adverse cognitive effects. There have been no well-established pharmacological approaches to attenuating adverse cognitive effects, although there is interest in using *N*-methyl D-aspartate antagonists, such as ketamine and thyroid hormone.

Perhaps because subjective memory correlates best with mood and the majority of patients respond to ECT in systematic research, most patients seen in these settings report improved cognitive function post-ECT. It has been difficult to distinguish these patients from controls in the subjective assessment of memory months after ECT in randomized, controlled trials; in community settings, which are characterized by the inclusion of a broader range of patients and ECT techniques, subjective complaints of memory impairment are more frequent. Nonetheless, generally favorable attitudes are expressed by patients who have received ECT, especially compared to attitudes of the general public, and the majority of patients would have treatment again if necessary.

Other Adverse Effects

Postictal agitation has an undefined etiology but can be associated with various factors, including bilateral electrode placement, lower anesthetic dosage, concomitant use of medications, and anxiety or agitation pre-ECT. Although fleeting in severity, the more severe forms require emergent management with increased stimulation, medications such as short-acting benzodiazepines, lighter and ECT anesthetics, and even restraints. Prophylaxis may include switching electrode placement to unilateral, increasing the dose of anesthetic agent pre- and post-ECT, modifying the dose of succinylcholine to prevent awakening while paralyzed or to decrease lactate generation, and alteration of medication regimens to address agitation by the use of neuroleptics.

ECT also may be associated with a number of less serious, although uncomfortable side effects. Headaches and nausea occasionally occur postictally. Headache has been reported to occur in up to half of all patients, although the

...ure seems unrealistically high. The etiology of postictal headache is unknown, and ascertaining cause is complicated by the presence or withdrawal of medications and the fact that anxiety often accompanies target illnesses for which ECT is used, such as depression. The throbbing quality of the headache suggests a vascular component, and migraineurs certainly seem more vulnerable to developing this side effect. Symptomatic management with analgesics, including nonsteroidal anti-inflammatory drugs, is often sufficient, but use of these agents prophylactically—for example, intravenous ketorolac—may be required. Migraine sufferers may need to use triptans posttreatment.

Nausea may accompany headache or occur alone in a minority of patients. Again the etiology is complex, including the use of anesthetic agents. Antiemetics, including dopamine antagonists such as Compazine, can be employed symptomatically. Occasionally, a 5-HT_3 antagonist such as ondansetron may be needed to control discomfort.

INVESTIGATIONS IN ELECTRICAL BRAIN STIMULATION TREATMENT

There is interest in continued refinements of ECT techniques. Common themes in these approaches are focusing the treatment spatially to optimize dosing in brain areas associated with putative neural networks involved in depression and other psychopathologies that are indications for ECT and to diminish dosing in areas associated with adverse cognitive effects, and improving the efficiency of a noninvasive electrical stimulus in direction and amplitude, even to a subconvulsive level. This research is parallel to investigations in magnetic stimulation (e.g., repetitive transcranial magnetic stimulation) and to the renaissance of invasive electrical techniques (e.g., vagal nerve stimulation and deep brain stimulation).

SUGGESTED CROSS-REFERENCES

See Section 1.2 on functional neuroanatomy, Section 1.15 on basic and applied electrophysiology, and Section 1.7 on neurotrophic factors. See Section 31.35 on neurosurgical treatments and deep brain stimulation and Section 31.34b on other brain stimulation treatments. Also see Section 54.4f on ECT in geriatric psychiatry.

References

American Psychiatric Association: *The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging—A Task Force Report.* 2nd ed. Washington, DC: American Psychiatric Press; 2001.

...LS, Haskett RF, Mulsant BH, Greenberg RM, Prudic J: Determinants of seizure threshold in ECT: Benzodiazepine use, anesthetic dosage, and other factors. *J ECT.* 2000;16:3.

...elli A, Dell'Osso L, Tundo A, Pini S, Chiavacci MC: Electroconvulsive therapy in medication-nonresponsive patients with mixed mania and bipolar depression. *J Clin Psychiatry.* 2000;62:552.

...MA, Aliei Y, Augoustides JG, O'Reardon JP: Uncommon but serious complications associated with electroconvulsive therapy: Recognition and management for the clinician. *Curr Psychiatry Rep.* 2008;10:474.

Devanand DP, Dwork AJ, Hutchinson ER, Bolwig TG, Sackeim HA: Does ECT alter brain structure? *Am J Psychiatry.* 1994;151:957.

... WM, Rasmussen KG Jr: Effects of general anesthetic agents in adults receiving electroconvulsive therapy: A systematic review. *J ECT.* 2008;24:208.

...A, Suing MM, Schweitzer I: Cognitive side effects of brief pulse electroconvulsive therapy: A review. *J ECT.* 2008;24:3.

... CH, Knapp RG, Petrides G, Rummans TA, Husain MM: Continuation electroconvulsive therapy vs pharmacotherapy for relapse prevention in major depression: A multisite study from the Consortium for Research in Electroconvulsive Therapy (CORE). *Arch Gen Psychiatry.* 2006;63:1337.

... SH, Maddox JH, Prudic J, Devanand DP, Sackeim HA: The effects of electroconvulsive therapy on memory of autobiographical and public events. *Arch Gen Psychiatry.* 2000;57:581.

... WV, Reboussin DM, Weiner RD, Sackeim HA: Titrated moderately suprathreshold vs fixed high-dose right unilateral electroconvulsive therapy: Acute antidepressant and cognitive effects. *Arch Gen Psychiatry.* 2000;57:438.

...ke S, Sackeim HA, Schaur DB: Electroconvulsive therapy of acute manic states: A review of 50 years' experience. *Am J Psychiatry.* 1994;151:169.

Nobler MS, Sackeim HA, Prohovnik I, Moeller JR, Mukherjee S: Regional cerebral blood flow in mood disorders, III. Treatment and clinical response. *Arch Gen Psychiatry.* 1994;51:884.

Olfson M, Marcus S, Sackeim HA, Thompson J, Pincus HA: Use of ECT for the inpatient treatment of recurrent major depression. *Am J Psychiatry.* 1998;155:22.

Painuly N, Chakrabarti S: Combined use of electroconvulsive therapy and antipsychotics in schizophrenia: The Indian evidence. A review and a meta-analysis. *J ECT.* 2006;22:59.

Perera TD, Luber B, Nobler MS, Prudic J, Anderson C: Seizure expression during electroconvulsive therapy: Relationships with clinical outcome and cognitive side effects. *Neuropsychopharmacology.* 2004;29:813.

Prudic J: Strategies to minimize cognitive side effects with ECT: Aspects of ECT technique. *J ECT.* 2008;24:46.

Prudic J, Olfson M, Marcus SC, Fuller RB, Sackeim HA: Effectiveness of electroconvulsive therapy in community settings. *Biol Psychiatry.* 2004;55:301.

Prudic J, Peyser S, Sackeim HA: Subjective memory complaints: A review of patient self-assessment of memory after electroconvulsive therapy. *J ECT.* 2000;16:121.

Rasmussen KG, Rummans TA, Richardson JW: Electroconvulsive therapy in the medically ill. *Psychiatr Clin North Am.* 2002;25:177.

Rey JM, Walter G: Half a century of ECT use in young people. *Am J Psychiatry.* 1997;154:595.

*Sackeim HA, Haskett RF, Mulsant BH, Thase ME, Mann JJ: Continuation pharmacotherapy in the prevention of relapse following electroconvulsive therapy. *JAMA.* 2001;285:1299.

Sackeim HA, Long J, Luber B, Moeller JR, Prohovnik I: Physical properties and quantifications of the ECT stimulus: I Basic principles. *Convulsive Ther.* 1994;10:93.

*Sackeim HA, Prudic J, Devanand DP, Nobler MS, Lisanby SH: A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. *Arch Gen Psychiatry.* 2000;57:425.

Sackeim HA, Prudic J, Fuller R, Keilp J, Lavori PW: The cognitive effects of electroconvulsive therapy in community settings. *Neuropsychopharmacology.* 2007;32:244.

*Sackeim HA, Prudic J, Nobler MS, Fitzsimons L, Lisanby SH: Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *Brain Stimulation.* 2008;1:71.

Schmidt EZ, Reininghaus B, Enzinger C, Ebner C, Hofmann P: Changes in brain metabolism after ECT-positron emission tomography in the assessment of changes in glucose metabolism subsequent to electroconvulsive therapy—Lessons, limitations and future applications. *J Affect Disord.* 2008;106:203.

Shiwach RS, Reid WH, Carmody TJ: An analysis of reported deaths following electroconvulsive therapy in Texas: 1993–1998. *Psychiatric Serv.* 2001;52:1095.

Shorter E, Healy D: *Shock Therapy: The History of Electroconvulsive Therapy in Mental Illness.* Piscataway, NJ: Rutgers University Press; 2007.

*Tharyan P, Adams CE: Electroconvulsive therapy for schizophrenia. *Cochrane Database Systemic Review 2.* 2002:CD000076.

31.34b Other Brain Stimulation Methods

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INTRODUCTION

Brain stimulation in psychiatric practice and research uses electrical currents or magnetic fields to alter neuronal firing. There is a growing list of tools capable of eliciting such neuromodulation, each with a different spectrum of action. These tools either apply electrical or magnetic fields transcranially or involve the surgical implantation of electrodes to deliver electrical currents to a cranial nerve or to the brain directly. The transcranial techniques include cranial electrical stimulation (CES), electroconvulsive therapy (ECT), transcranial direct current stimulation (tDCS, also called direct current polarization), transcranial magnetic stimulation (TMS), and magnetic seizure therapy (MST). The surgical techniques include cortical brain stimulation (CBS), deep brain stimulation (DBS), and vagus nerve stimulation (VNS). These methods are shown in Figure 31.34b–1 and defined in Table 31.34b–1. ECT and DBS are discussed in separate sections of this book.

The historical roots of brain stimulation in psychiatry can be traced to the introduction of ECT in 1938 by Ugo Cerletti and Lucio Bini. Since then, electrical methods for neuromodulation have been in continuous use in psychiatry. ECT, which uses alternating electrical